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A PHYSIOLOGIC ANALYSIS OF THE NATURE AND OF THE TREATMENT OF BURNS

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THE PURPOSE of this communication is to discuss some of the local physiologic changes in and about burns and certain physiologic requirements necessary for the rational treatment of these injuries. On the basis of this discussion it becomes possible to review a method of treating burns designed to meet these requirements and proven efficacious both in the laboratory and in the clinic.

The local treatment of burns necessitates consideration of three fundamental lesions: (1) Injury to the epithelium; (2) injury to the vascular bed, particularly the capillaries in the burned area; and (3) injury to the surrounding and supporting tissues. Each is a distinct lesion characteristic of the tissue affected, and each is vitally concerned in the ultimate healing of the wound. Naturally, consideration of any one of these lesions requires appraisal and consideration of the other two. It is believed that the underlying cause for the lack of uniformity in the treatment of burns has been failure to appreciate this triad of lesions and the physiologic changes brought about by them. For example, injury to the epithelium is the most obvious lesion in burns, and the one which has received most attention is local therapy. But with this go increased capillary permeability and injury to supporting tissue.

THE GENERAL NATURE OF A BURN OF THE SKIN

In a burn the extent of injury to individual cells is relatively constant over an appreciable surface area, and beyond this there are cells damaged, more or less, dependent upon the length of exposure and the degree of heat applied. These gradations of injury interfere somewhat with experimental observations in which it is desired to create a very constant and repeatable burn. The inevitable differences in degree of injury are important, however, not only from the pathologic standpoint but from the physiologic standpoint as well, since degree and persistence of physiologic reactions will depend upon the severity of the pathologic changes in the tissue. Depending upon their severity, burns produce varying degrees of systemic effect, but the

cause, or causes, of these serious effects upon the patient have not been identified satisfactorily. Extensive studies on the blood have revealed but few changes in the known chemical constituents. Elevation of protein metabolism following severe burns has been known for some time. French workers[1] recognized a large amount of undetermined nitrogen in the blood of badly burned patients and attributed this to "polypeptides." Other workers[2, 3] in this country doubt this suggestion. Taylor, and his coworkers[3, 4] have recently made a thorough study of protein metabolism in severely burned patients. They attributed their findings of an irreversible azotemia with a large amount of undetermined nitrogen to an increased rate of protein catabolism plus a partially damaged kidney. They found this type of azotemia chiefly in patients who also showed hemoglobinemia and hemoglobinuria. They made the interesting and important observation that severely burned patients lost large amounts of nitrogen in the urine and that more than four times the normal protein intake was necessary to keep them in positive nitrogen balance. Perlmann, Glenn, and Kaufman[5] described the appearance of a new globulin fraction in lymph collected directly from the burned extremity in calves. It is not known as yet just what significance can be attached to this finding, but it is certain that it is in some way related to the thermal injury and that the new globulin comes directly from the burned area. Muus and Hardenbergh[6] have reported that lymph collected from lymphatic trunks draining severely burned skin and subcutaneous tissues in calves and dogs contains a substance which increases the oxygen utilization of slices of liver from normal rats. This substance is of unknown composition. It is not the globulin described by Perlmann, and her associates, since that compound does not affect oxygen utilization. The finding of something in the exudate from burns, which is precisely what the lymph utilized by Muus and Hardenbergh is, must prove of value in understanding both the local and the general changes induced by burns. Animals severely burned, but with no break in the skin, often display a mounting temperature and may die with hyperpyrexia 8 to 15 hours after the injury. The same observation has been made upon human patients and is in no way related to infection. The fact seems to be that if a burn is extensive enough and circulatory conditions, including the lymphatic side of the process, provide thoroughgoing absorption, something, perhaps essential for local healing, leaks over into the circulation and produces systemic effects which may be highly undesirable. One must keep this in mind in treating the shock so frequently attending severe burns, since the routine employment of external heat may be exactly the wrong thing to do, just as Blalock[7] has demonstrated in the treatment of traumatic shock.

The loss of sodium from the blood into injured tissue has been suggested by Fox and Keston[8] as the chief cause of the diminished plasma volume in surgical shock from all causes. Fox[9] gave large amounts of 1.75 per cent sodium lactate orally to patients with "extensive full-thickness" burns. In view of the implied severity of the burns this would seem a favorable result,

but this form of treatment and particularly the evidence behind it require much more study before reliance can be placed upon them.

SPECIAL CHANGES IN BURNS

1. THE EPITHELIUM

The primary function of the epithelium is protection of the underlying structures. The protective covering does not consist of the epithelium alone but, in addition, a much thicker and tougher layer between the epithelium and the subcutaneous tissue below. This subepithelial layer of skin is made up of white fibrous tissue containing in its meshes the capillaries and lymphatics of the skin and in addition the very important hair follicles, sebaceous and sweat glands. One of the first results of increased capillary permeability in the skin is the accumulation of extravascular fluid in the superficial tissue spaces beneath the basement membrane and ultimately, due to pressure from below, the epithelial layer is lifted off and a blister is formed.

Simple destruction of the epithelium constitutes a minor or second degree burn. The great majority of these if treated with any care whatever will heal uneventfully. Reëpithelization arises from the margins of the wound and from the very important hair follicles in the deeper layers of the skin. Howes[10] has shown by colored photography that reëpithelization of a denuded area from the margins of a wound or from an island of epithelium in the wounded area proceeds at the rate of about 0.5 Mm. a day after a latent period of four to six days. At such a slow rate, reëpithelization of a large surface would take a very long time if it were to come from the margins of the burn alone. The preservation of the islands of epithelium in the hair follicles lying deep in the corium, undestroyed by the original injury, is a matter of great importance. The chief factors concerned in the destruction of these islands should be appreciated and every effort made to avoid them. They are, namely, (1) too active cleansing or scrubbing of the part at the time of the initial débridement; (2) the application of harmful local therapy;[11] (3) infection; and (4) inordinate swelling of the subcutaneous tissue with resultant stretching of the skin and anoxia of these cells, especially in poorly vascularized areas or in areas where the skin is very thin.

2. THE VASCULAR LESION

The effect of heat upon the finer blood vessels, arterioles, capillaries, venules, and arteriovenous anastomosing branches is of major importance in estimating the severity of burns and in understanding current therapeutic measures.

Essentially, the effect of heat upon capillaries, short of thrombosis and destruction, is dilatation with increase in permeability. The reaction in viable vessels is apparently brought about in two ways: First, through stimulation of the pain nerve endings in the skin, there is a dilatation of the adjacent capillaries and arteriovenous anastomoses in the burned and immediately adjacent tissue—the axone reflex. This is a reversible reaction

depending upon cessation of stimulation of the pain nerve endings. The nervous effect is perhaps due to histamine or histamine-like substances released as the heating of the tissue occurs. It is probable that still other and more stable chemical compounds, occurring in the injury as dead tissue is removed and recovery begins, are also dilator in effect and maintain the increased local blood supply far beyond the primary opening of the vessels. Local vascular changes such as these should be looked upon as essential provisions for healing, since they assure maximum oxygenation and supply of nutrient substances from the blood. At the same time, one may conceive (it is not proved) that if very severe burns release vasodilator compounds into the general circulation, even in small amounts, these same substances which are so essential locally may induce a general and extremely slight degree of increased permeability of capillaries which would assist in lowering plasma volume and inducing shock.

Second, and more important, there is the direct effect of heat upon the capillary wall. This, too, is reversible if the burning temperature has not been actually destructive. McCarrell[12] showed that if the temperature of the mucous surface of the nasopharynx did not get above 55° C. dilatation and increased capillary permeability disappeared fairly promptly. Exposure to temperatures above this results in a progressive delay in recovery of the capillary endothelium. It has been demonstrated[13] that viable capillaries injured in a severe burn ceased to leak abnormally in about six days following the injury, if no infection was present. Injury to the capillary endothelium by the application of heat is not the sole cause for the perpetuation of increased capillary permeability. Once swelling of the tissues has begun, capillaries present in loose tissue, where a large amount of swelling and stretching of the tissues may occur, tend to remain dilated through the stretching of their walls by the attached supporting tissues and through anoxia if any cause of stasis has been present.

A final factor that tends to perpetuate capillary leakage, and one that accompanies injudicious treatment of the shock that follows the initial fluid loss, is intravenous therapy. Harkins,[14] Blalock,[15] and others, have called attention to the disproportionate amount of fluid injected intravenously, even whole blood, that an area, with incompetent widely dilated capillaries, may receive. Salt solutions lacking protein are doubly injurious in that not only do they leak into the burned area in large amounts, but carry intravascular protein with them.

The changes in the amount and character of the extravascular fluid in the burned area as contrasted with sound tissue form a very important characteristic of burns and are directly related to the injury of the capillary endothelium. In burns one thinks of a large amount of tissue destruction. With this there should be a concomitant release of thromboplastic substance from the damaged cells with a resultant prompt clotting of the plasma-like exudate in the burned area. This conception would follow Menkin's theory of the localization of inflammation by irritants causing cell destruction

and blockage of drainage by coagulation in the tissue spaces and lymphatics. It has been shown,[16] however, that in burns caused by immersion of a part in boiling water, the extravascular exudate does not clot promptly but flows in profuse amounts through open lymphatics back to the general circulation. It is not until some hours later that general clotting of this exudate occurs. This delay in clotting or localization of the burn exudate may be due to one or all of the following factors. In the first place, in a burn there is often a delay in the breakdown of the killed and injured cells. This may be due, in turn, to sterile coagulation of cells, or to destruction by heat of the normally present preenzyme in the burned area, as suggested by Whipple.[17] In the second place, the comparatively minor burn to the deeper tissues even in a severe surface burn may result in widespread capillary dilatation without necessarily causing tissue destruction sufficiently severe for the release of thromboplastin. Although severe damage is done to the superficial tissues, the undersurface of the skin is amply supplied by capillaries which dilate widely, as is easily demonstrated by the intravenous injection of the colloidal dye T-1824 following a burn, and leakage from these capillaries passes easily into the loose subcutaneous tissue below, where, owing to little cell destruction, the supply of thromboplastin may be very small. The third factor is the finding in calves[2] of a great delay in the clotting time of lymph collected from a burned area in the first two to four hours after the burn. This suggested the possibility of an antithrombic substance produced in the burned area.

Prompt clotting of the extravascular exudate can be brought about at any time following a burn by the injection of thromboplastin, normal fresh muscle or other tissue ground in salt solution, into the burned area. Blockage of the lymphatics occurs immediately, with cessation of lymph flow. Capillary permeability does not stop, however, and the part swells even more rapidly as blockage of the return of the plasma-like exudate to the general circulation by way of the lymphatics has been accomplished. The swelling in the subcutaneous tissue is not confined to the burned area, but may spread for considerable distances through normal tissue as the pressure increases in the burned area. This spread is evident even when clotting of the burn exudate is prompt. Strict localization of the exudate is not possible even by artificially hastening and extending coagulation. Conversely, Glenn, Peterson, and Drinker[16] found that by heparinization prior to burning so that no clotting could occur, there was negligible swelling of the part with almost complete return of the plasma lost from incompetent capillaries to the general circulation *via* wide-open lymphatics.

These remarks on the vascular lesion in burns and the extravascular exudate are important in many very practical ways. They indicate that capillaries are extremely heat sensitive; that they react to heat by dilatation; that their recovery may be delayed for many days, and during this time leakage from them can continue in abnormally large amounts; that the use of intravenous plasma or other solutions must be accompanied by realization of

their transient beneficial effects as long as the capillaries remain permeable, the apparent recovery from shock following intravenous therapy being only transitory with the patient slipping back into a dangerous state shortly after the plasma infusion is stopped. The failure of the extravascular exudate to be promptly and effectively localized by clotting allows for maximum absorption of abnormal substances from the burn into the general circulation during the first six to ten hours, together with soluble therapeutic agents applied locally, and for the spread of contaminating bacteria and their products. When clotting of the exudate has taken place it becomes a stagnant gel, acting as a foreign body slowly disposed of and requiring complete removal before healing can take place. In addition, this clotted plasma produces an abnormal environment for the surrounding tissue cells, mechanically stretching or compressing them, often, we believe, to the point of anoxia and death, especially in the superficial less distensible part of the skin. The subcutaneous mass of clot forms an excellent medium for the growth of bacteria, becoming the source itself of abnormal products, and finally acting as a support and source of nitrogen for the proliferation of fibroblasts with ultimate extensive scarring. Restriction of the volume of exudate is imperative in all burns.

THERAPEUTIC REQUIREMENTS

Physiologically, certain definite therapeutic requirements present themselves. Simply stated these are: (1) A protective, noninjurious covering; (2) a method of control of capillary leakage; and (3) immobilization of the part.

It is not our purpose to discuss the pros and cons of eschars, simple nonpressure dressings, continuous or intermittent wet dressings. Suffice it to say that none of these methods meet either of the last two requirements, and, therefore, do not furnish adequate treatment of fresh severe burns.

1. THE PROTECTIVE COVERING

Of fundamental necessity are: First, that the dressing does no further damage to the burned surface. Cannon and Cope[11] have shown the advantage of using a simple bland ointment. They found that epithelization was delayed when either tannic acid or triple dye eschars were used. For their observations they used a single donor site of a split-thickness graft taken with the dermatome. Allen and Koch,[18] Siler and Reid,[19] Cope,[20] and others, employed gauze thinly impregnated with boric ointment. Owens[21] used sterile gauze soaked in physiologic salt solution, and, recently, Lund[22] has found that grease of any sort is detrimental rather than advantageous on the thin layer of gauze laid over burned surfaces and covered by plaster of paris.

Second, the covering must afford protection from contamination, since infection is one of the most difficult problems in burns. Howes[10] has shown that epithelial proliferation is greatly retarded by infection and that actual destruction of epithelium by bacteria or their products occurs. Hare[23] has

pointed out that a very dangerous source of contamination is from the unshielded noses and throats of persons attending these wounds. The recent work of the several clinics studying the effects of locally applied sulfonamides, reported by Meleney,[24] show that severe infections were twice as frequent in wounds with maximum initial washing as in those that had only minimum washing. This confirms the findings of Cope,[20] who practiced minimum débridement in the burns treated by him with satisfactory results. Levenson and Lund[25] have also employed minimum débridement with excellent results. It is important to note, however, that both Cope,[20] and Levenson and Lund,[25] employed types of pressure dressings and did not imply that their results would have been as good had they used eschars, where maximum débridement is a first necessity.

Third, the protective covering should require infrequent change. Howes[10] has shown that frequent dressings injure delicate advancing epithelial cells. Lund[26] called attention to the severe pain occasioned by the dressing of burns. Orr[27] is perhaps the greatest proponent of the principle of infrequent change of dressings. The danger of contamination of incompletely healed burns by frequent dressings is of paramount importance, and such dressings are contrary to sound surgical principles in the treatment of open wounds. As Paracelsus, in 1536, so wisely expressed it: "Warily must the surgeon take heed not to remove or interfere with nature's balsam, but protect and defend it in its working and virtue. It is the nature of the flesh to possess in itself an innate balsam which healeth wounds."

2. THE CONTROL OF CAPILLARY LEAKAGE

In 1941, Rhoads, *et al.*, reported the successful use of adrenal cortical extract in the treatment of capillary dilatation in burns. Recently, in 1943, these same authors,[28] reporting a much larger series of burns, came to the conclusion that as a routine measure adrenal cortical extract is not advised, as it does not control capillary permeability in the majority of burns. In an earlier part of this paper, the factors concerned in increased capillary permeability were discussed, and it is not surprising that such capillaries cannot be rendered normal by adrenal cortical extracts.

The credit for using external mechanical pressure as a means of controlling capillary leakage probably belongs to Blair,[29] who, in 1924, reported upon the efficacy of the pressure dressing in the successful grafting of skin. More recently, Allen and Koch[18] have used a similar dressing in the attempt to control increased capillary permeability in burns, although this principle was recognized many years before. The introduction of a mechanical attempt to control capillary leakage in the burned area is believed to be the greatest single advance in the local treatment of these wounds. The type of dressing applied by Allen and Koch may be termed the *external* pressure dressings, since the pressure is dependent upon cotton elastic bandages applied firmly over a thick buffer layer of waste cotton, gauze, or sponges. This dressing

has been used successfully by many, chief among whom are Allen and Koch,[18] Siler and Reid,[19] Owens,[21] Cope,[20] and others. Such a bulky dressing well applied also affords a fairly high degree of immobilization of the part. Its chief objection physiologically is that the treatment guesses at the amount of pressure necessary to control capillary leakage and consequent swelling. At best, the pressure applied is an estimate that will vary from operator to operator and from dressing to dressing. One must be careful not to produce either too much pressure or too little; the former is, of course, more dangerous than the latter. Another objection to this dressing is that it is difficult to hold accurately in the position of maximum function for prolonged periods without the danger of loosening of the bandage and loss of immobilization.

A second method of controlling capillary leakage by mechanical means is by use of a nonelastic and nondistensible dressing. This employs the principle of a rigid wall applied to conform exactly to the part as it exists at the time of the application. *No* external pressure whatever is used in the application, and the plaster of paris, the essential factor in the dressing, is as nearly skin-tight as possible, there being a very thin protective layer of gauze between the plaster and the burn. Thus, as plasma escapes from the dilated hyperpermeable capillaries, the extravascular tissue fluid pressure quickly builds up against the rigid encasement to exactly equal the pressure attempting to push the fluid out of the capillaries. In other words, once this pressure equilibrium has taken place, no more fluid can leak from the capillaries than can be carried away by lymphatics draining the part or absorbed by the capillaries in the burned area. Glenn, Gilbert, and Drinker[13] applied plaster encasements to the paws of dogs following a burn caused by immersing the part in hot or boiling water for definite periods. The first experiments were designed to test the efficiency of the blood circulation beneath a perfectly fitting skin-tight plaster. Liquid dental plaster, with a hardening time of five to seven minutes, was used. The burned paw was dipped directly into the liquid plaster and the encasement allowed to harden about the foot. Thus, between the encasement and the capillary wall there was an incompressible watery medium, so that literally the wall of the plaster became the wall of the capillary. Experiments were carried out over periods of recovery lasting from six hours to 15 days. Following the hardening of the plaster, the encased foot was removed from the metal container, the plaster dried, and another perforated metal can was slipped over the plaster and held in place with glue to prevent the encasement from breaking as the animal ran about on it. Studies included:

1. The testing of the skin temperature beneath the encasement over a period of 13 days, by the inclusion prior to encasement of a thermocouple next to the skin. There was at no time a decrease in the temperature in the burned and encased foot below that of the other unburned feet.

2. Measurement of venous oxygen in the veins from a burned and encased foot and a burned and nonencased foot. This revealed practically

identical oxygen saturation in both feet, and indicated a similar degree of dilatation of the capillary bed.

3. Measurement of lymph flow from a burned and encased foot and from a burned and nonencased foot. The drainage from the nonencased foot was much more profuse and indicated a greater number of open lymphatics in the stretched tissue of the nonencased foot as well as a much greater leakage of plasma from the capillaries in the nonencased foot. In addition to the decrease in the amount of lymph flow, there was a much more rapid blockage of the lymphatics and cessation of lymph flow from the encased foot, although in it the total amount of clotted exudate was minimal. Both of these factors are of considerable importance for absorption *via* the lymphatics in the early hours following a burn and the accumulation of large amounts of clotted subcutaneous exudate later on, as pointed out earlier in this paper.

4. Measurement of the end-lymphatic pressure in a burned and encased foot and a burned and nonencased foot showed that the pressure in the encased foot rose promptly to systolic blood pressure and varied only with systolic pressure. The pressure in the nonencased foot rose slowly, and usually some blockage of the lymphatics had occurred before maximum pressure readings were obtained. It is to be remembered that in the nonencased foot there is much room for dissemination of pressure through distention of the tissues, but unlike the encased foot the increased pressure is accompanied by stretching of the tissues. These experiments indicated to the authors that the pressure necessary to control capillary permeability was dependent upon the systolic blood pressure at the time the part was enclosed in a rigid dressing, and that this pressure was rapidly reached in the extravascular tissue spaces soon after the rigid dressing was applied.

5. Animals were allowed to survive with the encasements in place for one to three weeks. There was apparently no pain whatever and reëpithelization of the part occurred with great rapidity, with little or no scar tissue and no deformity even in very severe burns (45 seconds in 100° C. water). The plaster encasement dressing was changed to the roller bandage plaster dressing, and a number of equally successful experiments were carried out. Some points in the application of plaster necessary for the success of this technic are mentioned in the last section of this paper.

3. IMMOBILIZATION

The effect of motion on the movement of lymph and tissue fluids is well known. Drinker and Field[30] clearly proved that lymph flow is greatly enhanced by motion of any sort. Barnes and Trueta[31] performed a group of experiments in which they showed that toxic substances of sufficient molecular size not to be absorbed by the capillaries were prevented from reaching the general circulation in lethal doses *via* the lymphatics by immobilization of the injured part. Orr, again, is the great classical proponent of immobilization in the treatment of chronic infections. Lyons[32] felt that immobilization was largely responsible for the control of bacterial invasion

in a group of burns treated by minimum débridement. In burns, because of the possibility of deforming scars, the part should be immobilized in the position of maximum function. Contrary to the belief of some, immobilization over a period of three to six weeks does not result in contractures and difficulty in restoring function. Glenn, Gilbert, and Drinker found in their animals, and Levenson and Lund found in their patients, a very prompt restoration of normal function after immobilization for three to six weeks in plaster dressings. It is believed that early motion in burns is contrary to the principles governing healing of these wounds, and that until healing has taken place motion should be avoided and replaced by prolonged and complete immobilization in the position of maximum function.

4. THE CLINICAL USE OF CLOSED-PLASTER DRESSINGS

The aim of the animal experiments of Glenn, Gilbert, and Drinker[13] was to explore and demonstrate the physiologic requirements of local therapy. The actual application of these principles to human burns depended upon clinical trial and judgment.

Plaster application lends itself best to burns of the extremities. From the experience of Levenson and Lund,[25] and Barnes[33] it is probable that the clinical use of this method will be largely confined to the arms and legs, although others have applied encasements elsewhere. The after effects of severe burns of the hands are the most disabling injuries thermal agents can produce, and the use of plaster dressings in these cases is particularly indicated.

Glenn, Gilbert, and Drinker called attention to certain essentials in the application of the plaster dressing in burns that they had learned from the use of this dressing upon animals. They suggested that these principles be followed for the successful use of this technic in human burns:

1. The application of plaster must be with the minimum of padding, and *absolutely without* pressure. It is molded gently to the part.

2. The application of plaster to an extremity must extend entirely over the end of the extremity whether the end is burned or not. If this is not done, swelling distal to the encasement will occur and gangrene may result. This swelling is a result of relatively high venous and tissue pressure beneath the encasement. Venous blood in the normal area is under normal pressure and cannot return through the high pressure region beneath the encasement. At the same time, arterial blood can get through beneath the encasement into the normal part, and a one-way tourniquet with its disastrous effects results. Encasement of the normal area in the plaster bandage prevents this from happening as pressure beneath the plaster is equalized and no blockage of the venous return occurs.

3. The application of plaster must extend above the upper margin of the burn or swelling for a distance of two to four inches, otherwise a wedge of subcutaneous edema will develop at the upper end of the encasement, and marked swelling proximal to the encasement will occur.

Closed-plaster dressings have been used in human burns for the past ten years, but without full appreciation of the nicety of the method or its correct application. References to the literature will be found in papers by Barnes,[33] who has reported on the use of plaster similar in most respects to the method described in this report, and by Levenson and Lund[25] who have recently described the use of plaster dressings in the treatment of fresh burns of the extremity. Their work is of singular importance for they applied the plaster with an exact knowledge of what they wished to accomplish, which had been gained from experiments upon animals.

SUMMARY AND CONCLUSIONS

The outstanding points in the application of plaster to human burns as brought out by Levenson and Lund,[25] Barnes,[33] and my own observations are:

1. There is no local harm from this treatment.

2. There were no instances of injured circulation. Some may object to the application of plaster to a part that is certain to swell. In burns it is not the control of massive local hemorrhage through rupture of large vessels that one attempts to stop, but plasma leakage through a widely dispersed capillary bed. The safest way to restrain leakage seems to be complete encasement of the part in rigid plaster which holds blood vessels within the size present at the time of application and does not compress them by added increments of external pressure.

3. The prompt return of function of a part immobilized in plaster over prolonged periods has been one of the most gratifying features of this treatment. Recently, Levenson and Lund have been leaving their original dressing in place for as long as four weeks. Upon removal of the encasement, the return of full motion of the fingers or other points encased in plaster has been very rapid, requiring only a day or two.

4. Not the least important is the comfort obtained by this treatment. In nearly every instance the application of the initial dressing has been followed by a very prompt relief of pain. Occasionally, after a day or so, the patient may complain of a slight dull ache in the burned area. This does not persist, as a rule, and may be relieved by elevation, as suggested by Barnes,[33] and referred to in paragraph 8 in this summary.

5. Levenson and Lund found that the plaster dressing is easy to apply to human burns of the extremity. It is their impression that it can be applied more quickly and with more accuracy than other forms of pressure dressings they have used. Likewise, it is easier to teach others to apply.

6. The slight degree of after care of the burned area is one of the chief advantages of the plaster treatment. It is testified to by the practice of leaving the original dressing in place for as long as four weeks in severe burns. Patients with burns confined to the upper extremities may walk about or even be discharged from the hospital to come back for change of dressings. The importance of infrequent dressings of burns cannot be too greatly emphasized. Usually what prompts a change of dressing is not

the presence of definite clinical indications that local interference is necessary, but simply curiosity as to "how things are doing." Such curiosity must be restrained if one hopes to improve the treatment of these wounds. Not only is it not helpful, but it is definitely dangerous and injurious.

7. Débridement is minimal, with removal of only gross dirt and loose skin. No blisters were broken and sulfonamides were not used locally. Infection has proved localized and superficial. Fever, in burns limited to the hands and arms, was strikingly absent.

8. It is profitable to call especial attention to a statement in Barnes'[33] paper. He noted that pain or discomfort in an encased extremity occurring 24 to 36 hours after application of the dressing was relieved by elevation of the part. This simple observation calls attention to one of the causes of pain due to burns, namely, the process of distending and stretching the tissue and the sensory nerve filaments within them. Sensations interpreted as pain are most readily caused by change of stimulus at the site of impulse reception. That is, an irritant upon, or in, the tissues may cause pain when first introduced, but if the irritant remains exactly as applied pain gradually disappears. If pain is continuous or reappears after a period of comfort, something progressive, some sort of change has taken place. This fact applies directly to the closed plaster treatment of burns. A badly injured part subjected to plaster encasement is covered by a single layer of gauze and then by plaster of paris so as to hold it at exactly the volume existent at the moment of application and so as to prevent motion. The result of this prompt restraint of swelling and motion is to remove possible changes in state which will be perceived as pain. But let us suppose the surgeon has used a number of layers of gauze beneath the plaster. In a short time the part will swell so that no further change in volume is possible. Swelling ceases and pressure becomes equal through the part. At the same time the local hyperemia and abnormal leakiness of capillaries continues though actual release of fluid from them with storage in the tissues is prevented.

Recovery of capillaries will be progressive, those at deepest levels and heated least becoming normal first, and those nearest the surface and still viable being abnormally leaky for about a week. If, after 24 hours, the part is placed in a position which lowers venous pressure, it may begin to shrink away from the plaster, and then if it has happened to become slightly dependent, discomfort or pain may occur as it swells to fill the plaster casing. The same sort of analysis may be applied to burns received for treatment some hours after their occurrence. Swelling may already be maximal. In this case, the part should be elevated during the initial brief examination and cleansing and the plaster dressing applied. After this some degree of elevation may well be continuous for the first week, so that no preventable element of increased venous pressure may arrest shrinkage of the part under the plaster or cause abrupt increases in volume. In such cases it may be well to consider the use of the conventional pressure dressing, with the idea that even though one cannot know much about the pressure used or its consequences in

restricting capillary blood flow, it may be advantageous to employ an elastic covering which follows the size of the part. These are matters for further careful examination both in laboratory and clinic.

9. At the present time these directions for using closed-plaster dressings in the treatment of burns may be followed. After minimal cleaning and débridement and without breaking blisters, two layers of sterile gauze are laid over the burned surface extending above the area to be covered by plaster. If fingers are involved they are enclosed separately in the gauze. A thin sheet of roller plaster bandage is then applied to the part without pressure, extending over the end of the extremity and two to four inches above the burn. In mild burns the encasement is removed in seven to 14 days. In more severe burns it may be left in place for as long as four weeks. If the burn is incompletely healed or the epithelium is very thin, another encasement should be immediately reapplied. Grafting may be started as soon as the slough separates.

Numbness beneath the plaster is a positive indication for prompt removal. No cases of this have yet been observed, and if the principles for the correct application are adhered to, none should develop.

Infection beneath the encasement is usually well localized, and as a rule does not warrant removal of the encasement. Sulfonamides upon the burned surface are, at best, of questionable value.

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THE NUTRITIONAL CARE OF CASES OF EXTENSIVE BURNS*

WITH SPECIAL REFERENCE TO THE ORAL USE OF AMINO-ACIDS (AMIGEN) IN THREE CASES

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The nutritional status of extensive burns may be discussed under three headings: Loss of nitrogen; the change in plasma protein levels; and the nitrogen intake, which may include delayed blood and plasma transfusions.

Loss of Nitrogen: Lucido,[1] in 1940, published his metabolic studies on a case of burn estimated as involving 40 per cent of body area. He reported that the patient had a high urinary excretion of nitrogen for the first 25 days following the burn. An analysis of his published chart reveals that the output of urinary nitrogen was not consistent. The variations which occurred from day to day ranged between a maximum of 28 and a minimum of 10 Gm. per day. Browne[2] studied the nitrogen output in three cases of burns, one complicated by a fracture. On a regular diet all showed an elevated urinary output to as high as 28 Gm. per day, gradually dwindling down to normal on the 40th day to the 52nd. Taylor, Levenson, Davidson, Adams and McDonald,[3] in 1943, reported an excretion of as much as 45 Gm. of nitrogen in 24 hours, and called attention to the nitrogen deficit which would inevitably result from the cumulative loss. Cope, Nathanson, Rourke and Wilson[4] found that the level of nitrogen excretion in most cases of burns was comparable to that which occurs in normal persons, the highest amount which they reported being 22 Gm. (calculated from their published charts). The negative nitrogen balance was attributed by these workers to low intake; and the fact that the amount of nitrogen excreted was small appeared to be referable to absence of infections. Taylor, Levenson, Davidson, Browder and Lund,[5] in a later communication, reported one case of extensive burns, involving 45 per cent of the body surface in third-degree, and 10 per cent in second-degree burns, who excreted as much as 34 Gm. of nitrogen in the

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urine on some days. His published chart, when analyzed, showed an average excretion of 27.5 Gm. daily the first week, gradually declining but not reaching normal until the seventh week. None of these authors mentioned the possibility that the large early loss might be partly accounted for by hemoglobinuria, which was reported by Lucido and Taylor, and associates, as being present in their cases.

The Plasma Protein Level: The serum protein level in Lucido's case was 4.9 Gm. per cent on the third day following the burn, and gradually rose to between 5–6 Gm. per cent during the subsequent period of observation. Cope, *et. al.*, reported a total plasma protein level of 5.5 Gm. per cent for a burn involving 11 per cent of body surface on the 39th day. In the case reported by Taylor, *et. al.*, the level of total plasma protein fell to 3.1 Gm. per cent. Only 1.6 Gm. per cent of albumin was present, accompanied by massive edema, until strenuous efforts were made to increase the protein intake, when the level rose to only 6 Gm. per cent. These protein figures observed in the latter stages of burns clearly demonstrate the presence of hypoproteinemia.

In a still more recent communication, Taylor's group[6] showed that of 81 patients with burns who were studied, 40 had hypoproteinemia. This condition, moreover, seemed to have a definite correlation with the severity of the burns. In 12 having burns affecting between 10 and 50 per cent of the body surface, eight, or 75 per cent, showed progressive hypoproteinemia. In 51 cases with burns involving less than 10 per cent, however, eight, or 15 per cent, showed a reduction in the amount of plasma proteins.

The Nitrogen Intake: The maximum nitrogen intake of Lucido's case was 120 Gm. of protein (19 Gm. N) toward the end of his study period. Cope, *et. al.*, cases had intakes of from 10 to 32.5 Gm. of nitrogen per day, the latter figures being made up mostly of large transfusions. In Taylor, *et. al.*, cases, the intake fluctuated between 35 Gm. of protein to 100 Gm. a day, until the 12th week, when the low plasma protein mentioned above was found and "the clinical condition was desperate." Then the intake was increased by administering additional protein in the form of 75 Gm. of albumin units and several units of desiccated plasma intravenously and *per os* through a stomach tube. On some of the days of special treatments, the protein intake was as high as 500 Gm.

In regard to the problem of protein intake, Taylor's group,[6] in their most recent paper, state that:

> "In all burned patients admitted to this hospital, an attempt was made to meet the demand for protein by increasing the protein intake to from 100 to 125 Gm. a day. Even at this level, there was a marked negative nitrogen balance in nine patients with severe burns. Most of the patients with minor burns of less than 10 per cent of the body surface involved responded to the intake of 125 Gm. of protein a day with a return of their plasma protein to normal; but in those patients with a continued marked loss of nitrogen into the urine, this did not occur. Indeed, in some of the severely burned patients, it has been calculated that on the basis of the loss of nitrogen into the urine alone, 300

Gm. of protein a day would have been required to maintain nitrogen equilibrium. In addition to this loss, some patients continued to lose large amounts of nitrogen material from the burned surface for long periods of time. This insensible loss could not be calculated. The restoration of protein under these combined circumstances was a difficult problem, since the amounts required were considerably greater than those the patients could ingest."

The present work deals with the nutritional care of three cases of thermal third-degree burns of, respectively, 10, 30 and 50 per cent of body surface. The administration of a high caloric and high nitrogen intake as amino-acids (amigen) *per os* sufficed to maintain nutrition. The nitrogen balance was followed, for a varying period of time, throughout convalescence and the plasma proteins and body weight were determined periodically.

CASE REPORTS

Case 1.—J. C., male, age 53 (Table I), was admitted, February 7, 1943, with second- and third-degree burns of both hands and third-degree burns of face and head. On entrance, his burns were sprayed with sulfathiazole solution in another hospital, but on the next day he was transferred to the Bellevue Hospital where débridement was performed and vaselined gauze applied. On February 12, 1943, when he came under the care of the Nutrition Service, he had lost 4.5 Kg., his hematocrit was 48, and plasma protein level 4.7 Gm. per cent; cephalin flocculation test 3+++. He was given 500 cc. of plasma and immediately put on a diet consisting of 35 Gm. of nitrogen in the form of amigen, his caloric intake being 4500 daily. This intake was maintained with but slight variation throughout his stay in the hospital, a period which ended April 14. His nutritional state was excellent throughout his recovery. Thus, on February 23, ten days after he was placed on this diet, his plasma proteins had risen to 6.63 Gm. per cent, and his weight was 55.7 Kg., which was only 0.8 Kg. below his initial weight of 56.8 Kg. On April 14, with most of the burned areas healed, he weighed 62.5 Kg., or 5.7 Kg. above his initial weight.

TABLE I

J. C., male, 53 yrs., admitted 2/7/43: 2nd-3rd degree burns, both hands. 3rd degree face and head

			Nitrogen Output								
Date	Caloric Intake	N. Intake Gm.	Urinary N. Gm.	Dressing Gm.	Fecal N. Gm.	Total N. Output Gm.	N. Balance Gm.	P.P. Gm. Per Cent A/C	Hem.	Wt. Kg.	Remarks
2/6	Burned when falling into a fire, 10 per cent body surface, sprayed with sulfathiazole sol.										
2/7	Débrided										
2/12–14	9,756	74	24.33		4.42	28.75	+45.75?	4.7	48	52.2	2/12: 500 cc. plasma. ceph. floc. +++
2/14–17	13,250	99	51.98		6.63	58.61	+73.39?	2/15 6.39	2/15 47	2/17 53.7	2/17: ceph. floc. neg.
2/17–20	14,610	106.2	47.61		6.63	54.24	+48.36?	2/17 5.44	33		
3/20–23	14,610	106.2	36.79		6.63	43.42	+62.78?	6.63	2/23 38	2/23 55.7	Hb. 13 Gm.
3/23	14,610	106.2								58.8	Areas healing, excess granulat. in some areas
4/14	14,610	106.2						7.2	45	62.5	Referred plastic surgery for an old injured finger

Case 2.—J. McN., male, age 42 (Table II), was admitted June 29, 1943, with second- and third-degree burns on the right side of the trunk to midthigh, involving 30 per cent of body surface. He was débrided and vaselined dressings were applied. His weight on June 30, when his metabolic studies began, was 55.45 Kg. For the first five days, he received 24 Gm. of nitrogen and a caloric intake of 2600 a day. His urinary output during this period was roughly 17.5 Gm. per day, making an apparent positive nitrogen balance of 6.5 Gm. On the basis of these figures, he could afford to lose 6.5 Gm. of nitrogen per day in his exudate without utilizing his body nitrogen. This amount of intake was apparently insufficient, for his body weight on July 5 had fallen to 53.7 Kg. From July 4 to 7, his nitrogen intake was raised to 25.6 Gm., and in the period between the 7th and the 10th to 31.5 Gm., but his weight had fallen to 50.9 Kg. by the 10th. From the 10th on, his intake was raised first to 33.6 Gm. and then to 42.2 Gm.; and this latter intake was maintained until his discharge on October 2. On this increasing intake, his weight first stayed stationary and then went up, regaining and then, finally, topping his entrance weight. His plasma proteins showed a corresponding rise. His nutritional state was excellent throughout the rest of the convalescence.

TABLE II

J. McN., male, age 42, 2nd and 3rd degree burns, rt. side of trunk to midthigh (30 per cent of body surface)

			Nitrogen Output					P.P. Gm.			
Date	Caloric Intake	N. Intake	Urinary N.	Dressing	Fecal N.	Total N. Output	N. Balance	Per Cent		Hem.	Wt.	Remarks
		Gm.	Gm.	Gm.	Gm.	Gm.	Gm.	A/G			Kg.	
6/29–7/1	5,240	48	31.79		1.64	33.33	+14.67?	6/29	6/29	6/30	Vaselined gauze
								4.96	48	55.45	dressing
7/2–7/4	7,496	66	57.56		2.31	59.87	+ 6.13?	4.48	7/2		DTs
								7/2	42		
7/4–7/7	8,090	78	64.5		2.31	66.81	+11.19?			7/5	
										53.7	
7/7–7/10	9,770	94.5	55.35	15.46?	2.31	57.66	+36.84?			7/10	7/9: Burned areas
										50.9	healthy
7/10–7/13	10,520	100.7	70.03		2.31	72.34	+21.16?	7/12	7/12		
								5.89	45		
7/13–7/16	10,800	126.6	52.52		2.31	54.83	+65.67?				
7/16–7/18	7,200	84.4	37.57		1.54	39.11	+40.29?				7/15: 1.6 epithelized
7/16–7/20				14.22?				7/19		7/19	7/20: 40 per cent
								6.02	41	50.7	healed
										31.4	
7/22–7/17				14.92?				7/25	7/25	7/27	7/23: 50 per cent
								6.92	47	51.8	healed
8/3											80 per cent healed
8/2–8/ 7				4.44?							
8/27										55	
10/2										57.5	Healing complete

Attempts were made to collect the exudate from the burned surface. Since a great deal had seeped through the gauze dressings into the bedclothes, the nitrogen loss into the dressings is at best a minimum figure. It was 5.15 Gm. per day for the 8th to the 11th days.

Case 3.—M. W., colored, female, age 38 (Table III), suffered second- to third-degree burns on the trunk, right arm, buttocks, and left thigh on February 8, 1943. The burned area was estimated as involving 50 per cent of body surface, 90 per cent of the burns being third-degree. Her normal weight was 65.9 Kg. She was admitted in shock, was débrided, and tannic acid solution was applied. Between the date of her admission and April 16th, when she came into the Nutrition Service, she had 15 whole blood transfusions. She was also on the regular ward diet consisting of approxi-

mately 10 Gm. of nitrogen. On her admission into the Nutrition Service, her blood pressure was 90/50; and she was in very poor nutritional state, with a total plasma protein level of 4.31 Gm. per cent, hemoglobin 8 Gm., hematocrit 40. A 500-cc. transfusion of plasma was given. During the first three days of controlled study, she excreted 16.13 Gm. of nitrogen in her urine, averaging over 5 Gm. a day, a starvation level of excretion. She was then placed on 27.44 Gm. of nitrogen a day for three days, then increased to 36 Gm. daily for four days. Her urinary nitrogen during these two periods rose to 9 Gm. a day. Her apparent positive nitrogen balance rose from 3.5 to 24 Gm. a day. Her plasma proteins were 5.25 Gm. per cent; her hematocrit stayed at 39, and she showed no perceptible improvement, her weight on April 13th being 50.7 Kg.

TABLE III

M. W., female, age 38, 2nd-3rd degree burns, trunk, rt. arm, buttocks, left thigh, preburn wt. 65.9 Kg.

			Nitrogen Output					P. P. Gm.			
Date	Caloric Intake	N. Intake Gm.	Urinary N. Gm.	Dressing N. Gm.	Fecal N. Gm.	Total N. Output Gm.	N. Balance Gm.	Per Cent A/G	Hem.	Wt. Kg.	Remarks
2/8–2/9	Burned on 2/8, 30 per cent surface area, admission B/P 40/15, débridement and tannic acid spray										
2/9–4/6	15 blood transfusions 500 cc. each, regular ward diet.										
4/6–4/9	6,300?	30?	16.13				13.87?	5.31	40	50.9	Hb. 8 Gm.
4/9–4/12	9,465	82.32	23.96				59.36?				
4/13–4/17	15,135	143.85	37.73				106.12?	4/15 5.25	39	4/13 50.7	No perceptible improvement
4/18											500 cc. blood—25 per cent burned area grafted
4/19										51.3	Condition improving
4/21–4/23	9,500	99.00	18.94				80.06?	4/23 6.19	35		500 cc. blood—80 per cent grafts taking
4/28–4/30	9,500	99.00	14.18				83.82?				
5/2											Improving slightly
5/8–5/11	19,900	198	52.62	19.34?			145.38?				
5/17	6,550	66								53.57	Improving rapidly
6/15	6,550	66						6.8	42	59	Hb. 11 Gm. L. thigh and buttocks graft
6/30–7/22	6,550	66									Rt. shoulder and arm grafted
7/30	6,550	66								61.8	All grafts taking
8/10	6,550	66									
8/25	Amigen discontinued, put on high protein diet										
9/15										63.6	Most areas healed

She was given a blood transfusion in order to prepare her for the application of skin grafts to one-quarter of her burned area. Soon after the skin grafts were applied, her blood pressure fell to 80/40, a shock-like state which persisted until a blood transfusion was given. The significance of this will be discussed later in the paper. Her intake was increased to 35.77 Gm. daily and this continued for six days; *i.e.*, until April 19, when she began to improve and to show some gain in weight which was then 51.3 Kg. Her appetite improved and her intake was increased to 49.5 Gm. daily, at first, and then to 66 Gm., on which she improved rapidly, so that on May 17 her weight was 53.57 Kg. It may be mentioned that the exudate from the burned areas collected in the dressings in the four-day period between May 7 and 11 was found to contain 19.34 Gm. of nitrogen, or roughly 4.84 Gm. daily. These, again, are minimum figures, since some of the exudate was lost by seepage through the dressings. This minimal figure does not represent the amount lost in the areas not covered by the grafts, roughly, now 40 per cent of the body surface. On June 15, her plasma proteins were

6.8 Gm. per cent, and her weight 59 Kg., and hemoglobin 11 Gm. per cent. From then on, she ceased to be a nutritional problem.

Discussion: It appears that cases of burns of any appreciable extent of body surface tend to develop a state of malnutrition. The necessity for transfusions after the acute period is passed may be taken as rough index of the nutritional state of burn patients. Of the 38 cases reported by Cope's group, only five with burns over 20 per cent reached convalescence. On four of these the extent of the burned area ranged from 24.5 to 29 per cent of the body surface. The latter group required delayed transfusions of one to five units. The only instance on whom the blood protein level was reported was on a case in which 11 per cent of body area was involved. The plasma proteins on the 39th day were 5.5 Gm. per cent. In our Case 2, J. McN., in whom the burned area comprised 30 per cent of the body surface, as much as 4.5 Kg. was lost during the ten days following the accident. A plasma protein level of 4.48 Gm. per cent was noted on the third day and nutrition could not be maintained on 25.6 Gm. of nitrogen daily, an amount exceeding that of a classical high protein diet. Of the three cases available for study in whom over 50 per cent of the body surface was involved, Cope's case needed 25 transfusions during convalescence, and, inferentially, must have been in a precarious nutritional state. Taylor's case had lost 55 lbs. by the end of the third week, although already showing some improvement. The poor nutritional state of our Case 3, M. W., needs no comment. And in their latest paper, Taylor's group[6] reported that a loss of as much as 30 per cent of the body weight had occurred in some of the patients studied as a result of failure to maintain adequate nutrition.

When it is considered how many sources of nitrogen loss are present in burns, this poor nutritional status is understandable. There are at least four, perhaps five, avenues for this loss: (1) The intratissue loss into the burned areas, which may or may not be recoverable by the body; (2) the loss occurring in the exudate; (3) the loss as a result of hemoglobinuria; (4) the loss as a result of poor caloric and nitrogen intake consequent to anorexia; and (5) the possible loss due to a "antianabolic period" as a result of altered hormonal physiology.[7]

In this connection, Clowes, Lund and Levenson[7] reporting on 150 cases of burns, 109 of whom were victims of the Cocoanut Grove disaster, stated: "All patients with 10 per cent of surface area or more involved in third-degree burns became serious nutritional problems because of the loss of nitrogen in the urine and from the surface, and because of the increased nutritional requirements resulting from infection with fever."

Two preliminary attempts on our part to determine the protein loss in body exudates more quantitatively than in Cases 2 and 3 may be mentioned to illustrate how large this loss may become. Slabs of fine-pored cellulose sponges were used to collect the exudates. One case exuded as much as 0.42 mg. of nitrogen per square centimeter in 24 hours, while another case

of denuded surface due to avulsion, exuded as much as 2.26 mg. nitrogen per square centimeter. If half of the body surface of a man weighing 70 Kg., and 170 cm. in height, were to be involved in a burn, the 9,050 sq. cm. so involved would lose, according to one rate, 3.8 Gm. and according to the other rate, 19.9 Gm. of nitrogen in 24 hours. Three point eight grams of nitrogen would be 23.75 Gm. of protein, or the equivalent of 4,000 cc. of plasma; or of 114 Gm. of meat; and 19.9 Gm. of nitrogen would be equivalent to 124 Gm. of protein, over 2000 cc. of plasma, and 600 Gm. of meat.

The problem of keeping Case 1 in good nutrition was relatively simple. Cases 2 and 3 were somewhat more difficult. As it happened, the amount of nitrogen in the form of amino-acids fed to these three cases of increasing severity seemed to present a trend quantitatively in keeping with the extent of burns. Case 1 was kept in good nutritional state by 35 Gm. of nitrogen in the form of amino-acids. How much less might be required we are not in a position to know. Case 2, however, with the 30 per cent area burns could not be kept in good nutrition by 25.6 Gm. of nitrogen; while 33.6 Gm. maintained him, and with 42.2 Gm. he registered a rapid gain. Case 3 was not maintained by 36 Gm., but was maintained by 49.5 Gm., and registered a rapid gain with 66 Gm. It is quite possible that, as in the case of 35 Gm. for Case 1, so might 42.2 Gm. and 66 Gm. be supra-optimal for Cases 2 and 3. Table IV shows these amounts and their conversion values into meat and plasma. The amount of transfusion used in these cases was minimal, being *nil* in Cases 1 and 2, and only three transfusions were administered during the entire period of nutritional study in Case 3. It will be seen from the conversion table (Table IV) that to maintain a patient in good nutritional state under circumstances similar to our patients in Cases 2 and 3 with either meat feeding or plasma transfusion is almost an impossible task physically and economically.

TABLE IV

Patient	Original Body Wt. Kg.	Area Burned Percent	Total Daily N. Intake Gm.	N. in Gm. Wt. Kg.	Total Equivalents Proteins* Gm.	Meat* Gm.	Plasma* Cc.	Remarks
J. C.....	56.8	10	35	0.62	218.75	1093	3644	Sufficient
J. McN.....	55.45	30	24	0.43	130	750	2500	Insufficient
			25.6	0.46	160	800	2650	Insufficient
			33.6	0.61	210	1050	3500	Maintenance
			42.2	0.76	263.75	1318.75	4400	Rapid gain
M. W.....	65.9	50	27.44	0.42	171.5	857.5	4570	Insufficient
			36	0.55	225	1125	3750	Maintenance
			49.5	0.75	309.4	1485	5160	Slight gain
			66	1.00	412.5	2062.5	6875	Rapid gain

* Conversion table of nitrogen intake into proteins, meat and plasma. The assumption is made that meat contains 20 per cent protein, and the plasma, as now prepared, contains 6 Gm. per cent of proteins.

Thus, to feed a patient meat equivalent to the nitrogen intake of Case 3, M. W., would require the daily ingestion of about two kilograms of meat,

an impossible task. To give this amount of proteins in the form of plasma transfusions would require 23 units of plasma daily. The amigen corresponding to this nitrogen intake costs in the neighborhood of three dollars. The corresponding amount of meat would cost at least four times as much, while the cost of a corresponding amount of plasma would be prohibitive.

For this reason preparations, such as amigen, used in the three reported cases appear to be the solution to the problem of nutritional care in severe cases of protein drain. The rather logical way in which the dosages of amino-acids corresponded to the extent of the burned areas raises the hope that it might be possible to work out a practical formula of amino-acid feeding for burns of different extent.

The development of shock following immediately upon the first skin grafting in Case 3, M. W., is a phenomenon which may have an important bearing on the safety of this procedure in cases of extensive burns. Her plasma protein level at this time was 5 Gm. per cent. Theoretically, it is to be expected that in patients undergoing severe protein loss with protein synthesis barely keeping up with the loss, the opening up of new areas of the skin surface, with resulting increase in exudation and bleeding, would readily lead to the development of shock. If this explanation is correct, then patients in this condition should have no skin grafting attempted unless the protein nutrition has been improved and measures for the therapy of shock are at hand. The increase of the exudative surface would be at the highest point during the first two days before the graft has taken. Even after that, if all the graft has taken, the contraction of the graft would prevent this graft in the early stages from compensating for the exudation from the new donor areas.

SUMMARY AND CONCLUSIONS

1. The nutritional status of three cases of second- and third-degree burns involving, respectively, 10, 30 and 50 per cent of body area, given high caloric and high nitrogen feedings in the form of dextrimaltose and amigen were studied.

2. All three patients were maintained in excellent nutritional state.

3. There seemed to be a mathematical relationship between the extent of surface burned and the amount of nitrogen required to maintain nutrition.

4. Transfusions were reduced to a minimum.

5. Preparations such as amigen seem to be better tolerated and utilized than natural protein food and appear to be the solution to the problem of nutritional care of severe cases of protein drain.

6. The increased danger to patients with severe protein deprivation of the development of shock as a result of additional protein loss consequent upon opening up of new exuding areas in skin grafting has been discussed.

Grateful acknowledgment is made of the help of Dr. Stanley Sarnoff in suggesting the use of cellulose sponges for the collection of exudates and of that of David Gould in performing the palar planimetry.

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ADENOMATOSIS OF ISLET CELLS, WITH HYPERINSULINISM*

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WE have already reviewed (Whipple and Frantz, 1935) the studies which led to the recognition of islet cell tumors. Beginning with the original observation of Ssobolew, published at the same time as Schulze (1900), that ligation of the pancreatic duct was followed by disappearance of the parenchyma of the gland with the exception of the islets, there came in close succession a series of publications on hypertrophy of the islets in diabetes.

In 1904, Ssobolew described an hypertrophied islet in a diabetic. In 1905, Herxheimer found hypertrophy of the islets in five diabetics, and MacCallum confirmed this in two cases in 1907, and considered it compensatory. Cecil (1909) studied the pancreas in 90 cases of diabetes and found hypertrophy also. Dubreuil and Anderodias (1920) reported striking hypertrophy of the islets in a newborn child of a diabetic mother, and, in the same year, Horgan, in 262 autopsy specimens of chronic diseases of the stomach and biliary tract, looked for neoplastic changes associated with chronic pancreatitis and described three stages of hypertrophy of the islets, which he designated as primary, secondary, and tertiary "adenocytoplasia." In the tertiary stage he showed migration of cells through the connective tissue capsule, and considered this an "early neoplasia." In 1925, Boyd and Robinson described regeneration of islets in an insulin-treated case of diabetes—a child of nine, with an accidental death and postmortem examination. In 1926, Gray and Feemster reported compensatory hypertrophy and hyperplasia of the islets in another newborn infant of a diabetic mother. Womack and Cole (Case 2) (1937), reported a similar infant case, as did Bauer and Royster in the same year. This case was associated with tetany, and their report included a review of the literature. Somewhat contradictory conclusions have been reached by Potter, Seckel, and Stryker (1941). In discussing hyperplasia and hypertrophy of the islets of Langerhans of the fetus and of the newborn infant they say that such may be found "in the presence or in the absence of abnormal sugar metabolism in the mother and in the presence, or in the absence, of abnormal sugar metabolism in the infant itself." Benner, in 1941, reports a case of a newborn of a diabetic mother, dying 24 hours after birth, who showed a tremendous increase in the number and size of islets and morphologic evidence of gonadotropic stimulation.

Another observation is that of John (1931)—an insulin-treated case of diabetes, with complicating hyperthyroidism and cirrhosis of the liver, car-

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cinoma of the liver and gallbladder, and interstitial pancreatitis. Insulin was discontinued and the patient was readmitted in coma, with a blood sugar of 30 mg. per cent. Autopsy showed both atrophy and hypertrophy of islets, but the other pathologic findings make it impossible to be sure that the hypoglycemia antemortem was due to hyperinsulinism.

In 1924, Nuboer reported finding hypertrophy, islets 300–400 μ in diameter, both with and without diabetes, and suggested that most of the reported adenomas might not be true neoplasms but rather hypertrophy. The cases of adenoma reported up to that time had been those of Nicholls (1902) one case; Reitman (1905) one case; Herxheimer (1906), who found two in a case of diabetes; Morse (1908) two cases; and one case each by Helmholz (1907); Cecil (1911); Heiberg (1911); Alezais and Peyron (1911); Rollett (1912); Lecomte (1913); and Koch (1914). Priesel (1922) reported three cases, and Schneider (1924) two cases. In 1926, Warren reviewed these and added four of his own. He included as the twentieth case the report by Lang (1925), which is the first recorded case of nodular hyperplasia of the islets, called by the author "adenomatosis." The patient, a female, age 39, gave a history of attacks of depression, headache, abdominal pain and vomiting, occurring at intervals. No blood sugar determinations were recorded. At operation, a "tumor mass" involving the tail and most of the body of the pancreas was found, and a palliative gastro-enterostomy was performed. The patient died of bronchopneumonia and the islet adenomatosis was observed at autopsy, together with cholelithiasis, another finding possibly related to the clinical symptoms. The pancreas showed countless yellow nodules varying from 50–5,000 μ in diameter. These were encapsulated. There were no metastases. In none of the cases reported up to 1925, including this first case of adenomatosis, was there any definite clinical suggestion of hypersecretion.

In 1926, Herxheimer produced the first experimental hyperinsulinism by ligation of the pancreatic duct in a chicken. The result was hyperplasia of islets and an increase in the insulin content up to five or six times normal. The chicken died of hypoglycemia. Then came the first clinical case of hyperinsulinism with islet cell tumor (Wilder, Allan, Power, and Robertson, 1927) which, it will be recalled, had multiple nodules of infiltrating growth in the pancreas and metastases in liver, lymph nodes and mesentery, with a high insulin assay in the liver nodules.

In a second publication (Frantz, 1940) we have tabulated the cases with hyperinsulinism and tumor, benign and malignant, found at operation and at autopsy. In the literature since, there are records of additional cases. There are also four cases which we overlooked—three benign tumors which were cited by Cheley, Engel, and Nesselrode in the discussion of a paper by Thomason (1934), and one case of carcinoma with metastases, Jacobsen (1934). The statistics which follow are, therefore, corrected to include these.

In addition to these omissions and the cases which have appeared in the

literature since our 1940 review, we have 16 more cases in our own series explored for supposed hyperinsulinism. Of these one (Case 18) was a carcinoma, proved at autopsy at another hospital. Ballinger (1940) interpreted this as an islet cell carcinoma arising in aberrant pancreatic tissue in the liver. We are inclined to doubt this interpretation. At operation in this hospital, a mass was found in the retroperitoneal area between the upper border of the head of the pancreas and the spigelian lobe of the liver. It was a very large tumor, measuring 10 x 6 x 6 cm. Its upper limits appeared to infiltrate the liver, and the lower limits did not appear to be continuous with the pancreas. This we now feel should be regarded as a carcinoma arising in aberrant pancreatic tissue, behind and above the head of the pancreas where such aberrant structures have been described. In the detailed study by Faust and Mudgett (1940) of 370 cases of aberrant pancreatic tissue, none was found in the liver.

In five other cases of the 16 in our new series explored for hypoglycemia no tumor was found. One was a case of von Gierke's disease, so demonstrated at postmortem examination. In one case no tissue was removed. Eighteen months after operation this patient continues to hold the slight improvement she showed immediately, which is difficult to explain. She needs her meals, otherwise she has symptoms, but her fasting blood sugar has risen from 44 to 79 mg. per cent. In the remaining three, partial pancreatectomy was performed. In one of these, a girl of seven, half of the pancreas was resected. This showed, if anything, *hypoplasia* of islet tissue. She had no more convulsions after operation, but fasting blood sugar rose only from 42 to 56 mg. per cent. She was then lost to follow-up. The next case in which no tumor was found had a partial pancreatectomy. There was marked hyperplasia of islets but no neoplasia, and the patient was unimproved. He committed suicide three months after operation. The last case without tumor in Doctor Whipple's personal series (with operation, however, performed not at Presbyterian Hospital but at St. Luke's Hospital, New York City) had a partial pancreatectomy, without relief of symptoms. The pancreas showed nothing unusual.

In our series reported in 1940, 16 cases had been explored for hypoglycemia, in only one of which (Case 22) no tumor was found. Subsequent to the time the report was submitted for publication, this patient was re-explored (May, 1940) because of persisting symptoms. At the second procedure a tumor 1.7 cm. in diameter was found situated in the head of the pancreas, and was removed, with relief of symptoms.

Our series, therefore, now comprises 32 cases in all, in 27 of which tumor was found—one irremediable carcinoma and 26 operable cases. Four of these were reported in 1940 as having certain histologic characteristics suggestive of malignant tumor. Four more of the recent cases also show blood vessel invasion, making eight of the 26 under suspicion histologically. One of these, previously reported, was a postoperative death. The other seven are all

symptom-free; the earliest, and, incidentally, the one most characteristic of carcinoma histologically, being now a six-year arrest, and two others having gone more than five and four years, respectively, without return of symptoms.

Before completing the list of published cases to date, with our own added, we wish to present in some detail the histories of our own two cases of *adenomatosis*. Presumably, in both of these cases the same hyperplasia and neoplasia were present in the tissue left behind at partial pancreatectomy, and yet, to date, there has been no return of symptoms in either patient. The second case is very recent (only six months after operation) but as the first now has had no symptoms for 16 months, in spite of carrying heavy work in a war industry, it seems fair to report them both as similar.*

Case 25.—Dr. Allen O. Whipple: S. G., female, age 46, white, English. The patient was referred because of persisting symptoms following two operations. For five years before her admission to St. Luke's Hospital, in New Bedford, Mass., she had had spells of weakness and fainting, worse at the time of the menstrual period. These were somewhat relieved by benzedrin sulfate, and the patient herself noticed that candy would abort or shorten an attack. Administration of orange juice was observed to relieve an episode of semiconsciousness. At this time, the patient was moderately obese, weight 163 pounds. The rest of the physical examination was essentially negative. The fasting blood sugar, 12/24/41, was 23 mg. per cent. There were no other significant laboratory findings.

Operation.—February 24, 1942: Dr. Milton T. MacDonald, St. Luke's Hospital, New Bedford, Mass. Excision of adenoma of pancreas. This measured about 0.5 cm., and was found near the tail of the pancreas at its upper border.

Postoperative Course.—The patient felt somewhat improved for a few weeks and then began to manifest her old symptoms. Blood sugars were found as low as 40 mg. per cent.

Second Operation.—May, 1942: Dr. Milton T. MacDonald, St. Luke's Hospital, New Bedford, Mass. At this procedure a 0.75-cm. tumor was removed from the anterior surface of the pancreas, just below the superior border.

Second Postoperative Course.—The patient again improved for a short time, but blood sugars remained between 40 and 50 mg. per cent.

On admission to the Presbyterian Hospital, New York City, July 7, 1942, her weight was 165 pounds. Fasting blood sugar taken the next morning, with the patient found in shock at 6:30 A.M., was 34 mg. per cent.

Third Operation.—July 10, 1942: Dr. Allen O. Whipple. The abdomen was explored through a right rectus incision. The duodenum was mobilized for satisfactory palpation of the head of the pancreas. No tumor could be felt or seen. A partial pancreatectomy was, therefore, performed, with the removal of tail, body and a portion of the head.

Third Postoperative Course.—The patient made a good recovery, and had no return of symptoms 16 months after operation, in spite of heavy work on a milling machine, 48 hours a week. On her last follow-up examination, in November, 1943, her fasting blood sugar was found to be 90 mg. per cent, and her glucose tolerance test showed

* In connection with these two cases attention is called to the review by David, in 1940, of the results of pancreatectomy in hypoglycemia. We will not repeat these figures. A few other cases with operation *without tumor* may be added: Barnes and Richmond, 1935, Berry, 1935, Boone, 1934, Eagleston and Berkenbilt (Case 2) 1942, Fanta, 1937 (aberrant pancreas), Guerry and McCutcheon, 1936, Harris, 1938, Holman, Wood and Stockton (Case 4) 1943, Magner (Case 2) 1941, Quarrier and Bingham (Case 3) 1942, Reed, 1934, Rynearson and Walters, 1938, Smith, F. G., 1942 (aberrant), Wechsler and Garlock (Case 2) 1944, and Winans, 1933.

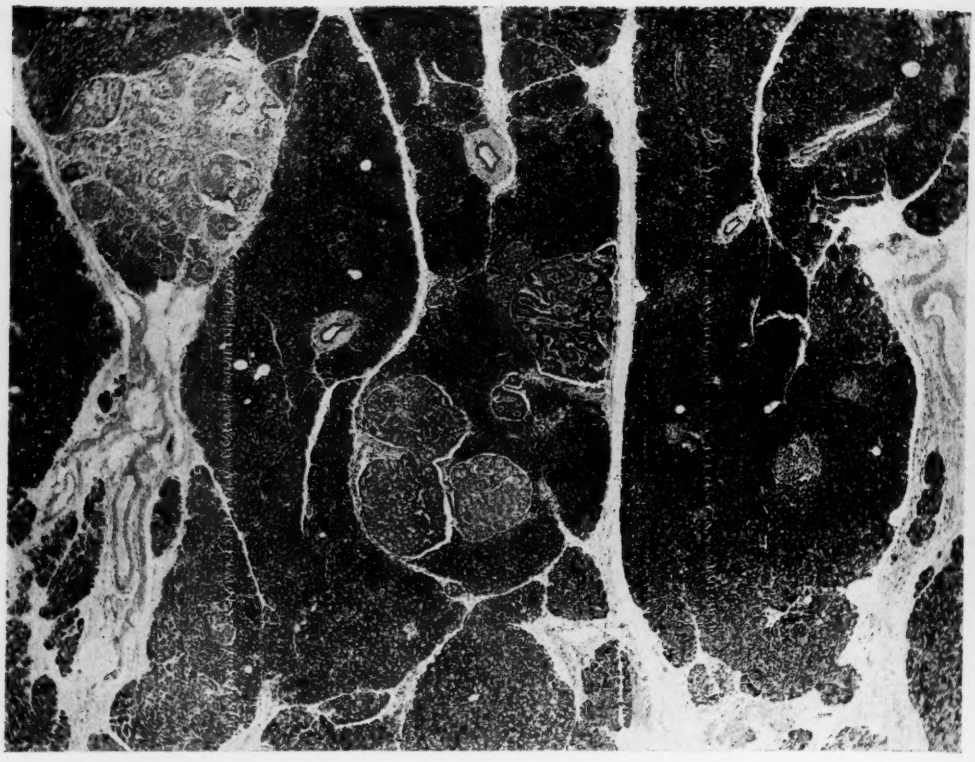

FIG. 1.—Case 1: Photomicrograph showing topography. Normal, hyperplastic and neoplastic islets ranging from 0.14 Mm. in greatest diameter.

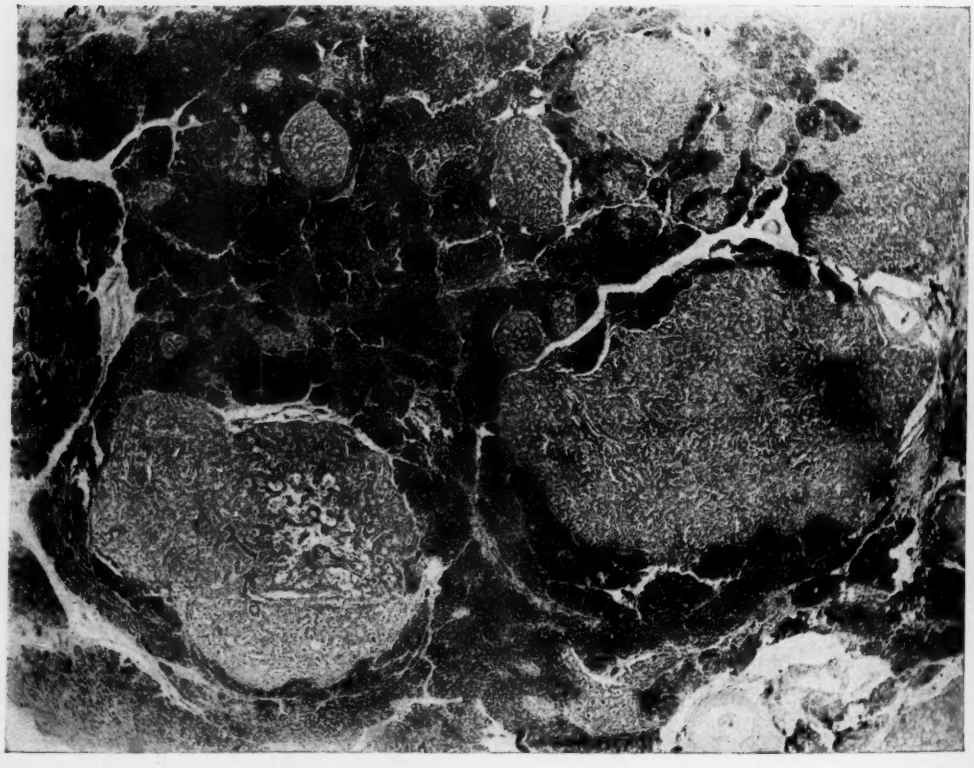

FIG. 1.—Case 2: Comparable field to Case 1. Islet diameters ranging from 0.14–2.4 Mm.

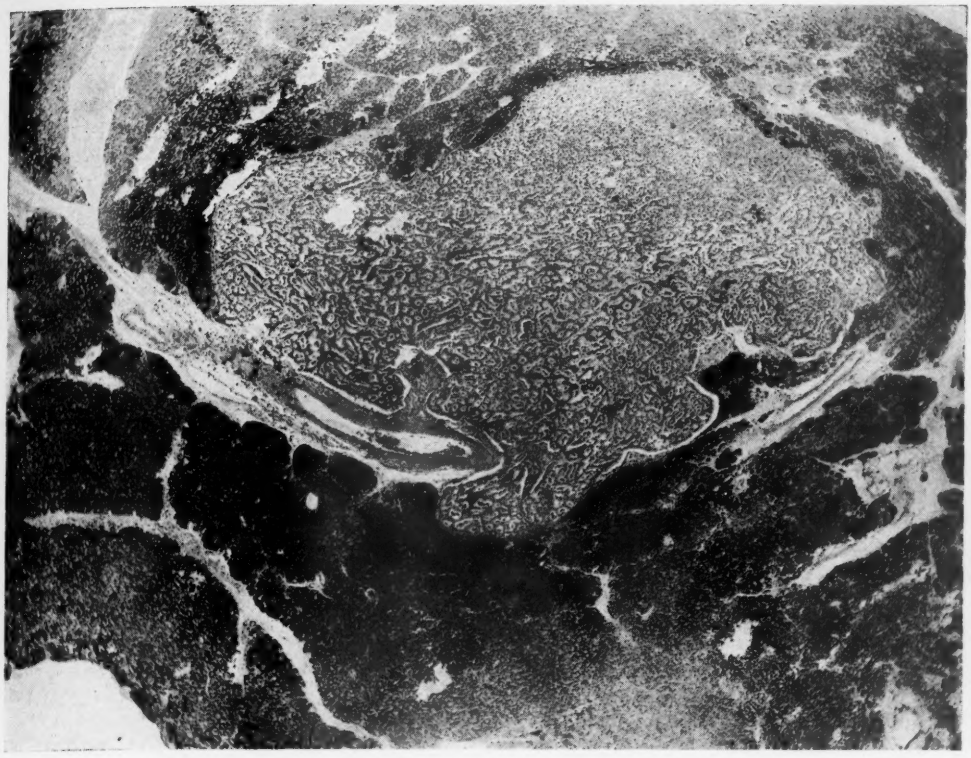

FIG. 2.—Case 2: Comparable field to Case 1. Macroscopic islet 4.0 Mm. in diameter.

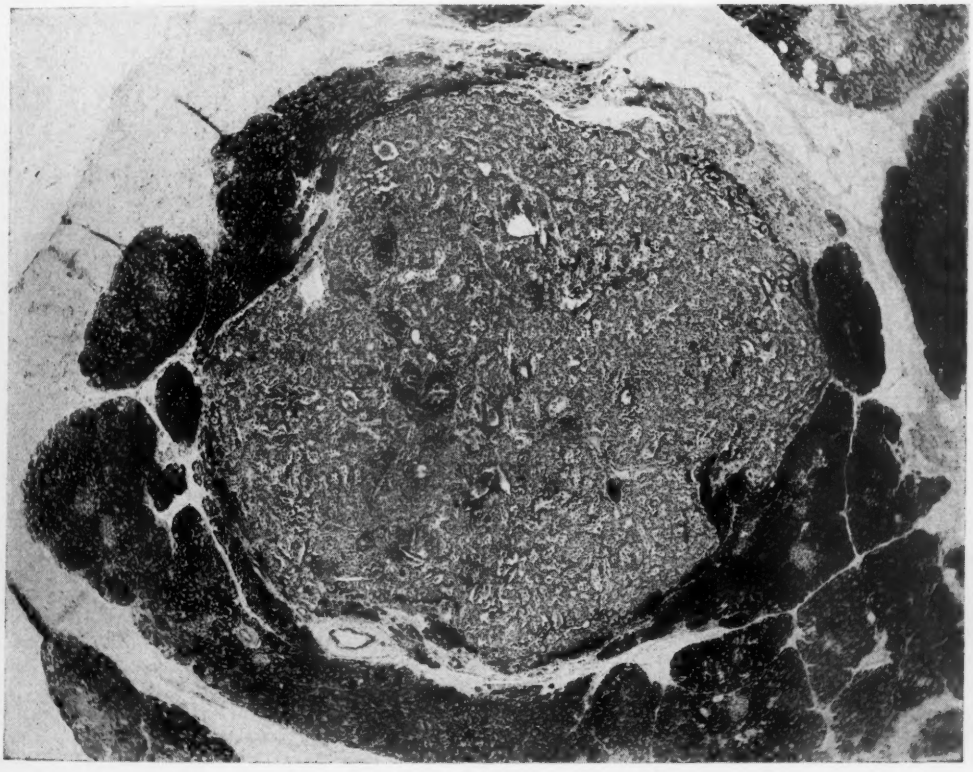

FIG. 2.—Case 1: Photomicrograph showing neoplastic islet 3.7 Mm. in greatest diameter.

figures all on the high side, with a diabetic type of curve. The patient had gained ten pounds and was advised to follow a 1200-caloric diet. She had not reported untoward symptoms since.

Pathologic Examination.—Gross: S. P. No. 82635. The specimen consisted of a segment of pancreas measuring 6.5 x 3 x 0.7 cm., and weighing, fresh, 8 Gm. A number of small purple or violet areas were seen on section, which were slightly raised above the surrounding yellow pancreatic tissue. These were considered as possible multiple adenomata when seen in the fresh state. They were discrete, but showed no striking capsule grossly.

After paraffin section, five discrete adenomata could be seen with the naked eye in hemotoxylin and eosin preparations on the slide. These measured 7, 5, 3, 3, and 2 Mm., respectively.

Microscopically, the sections showed adenomata of the ribbon type, similar to those described by Dr. I. M. Mason, Pathologist, St. Luke's Hosp., New Bedford, Mass., and were composed of islet cells, intimately associated with vascular spaces, some of which showed no endothelial lining. The adenomata were sharply demarcated, but not completely encapsulated. No mitotic figures were seen and no blood vessel invasion was recognized. In addition to these five macroscopic foci, there were many microscopic foci which were similar histologically, and, also, there were an unusually large number of normal and hyperplastic islets. Transitions were seen between these and the adenomata. In some of the small foci it was impossible to decide whether they should be considered hyperplasias or true neoplasms. (See photomicrographs)

Case 30.—Dr. Allen O. Whipple: O. T. V., female, age 46, white, American. The patient came to Vanderbilt Clinic, June 1, 1943, complaining of fainting spells of two years duration. These came on usually in the morning and lasted two to six hours. Return to consciousness was followed by severe headache and muscle pain. There was twitching occasionally during attacks and once she bit her tongue.

Physical examination was essentially negative except for cataract O. D. The condition, thought to be epilepsy, was not relieved by dilantin and phenobarbital. On a clinic visit, September 2, 1943, she volunteered the information that eating sugar helped her, and she was then admitted to the Neurological Institute for study.

At this time, she gave additional history of great irregularity in menstrual periods, a gain in weight of 90 pounds (130–220) since the birth of a child six and one-half years before, with gain most marked during the two years previous to admission, when fondness for sweets became more marked and when they were needed to ward off attacks.

Physical Examination: Height 5 feet 5.5 inches, weight 220 lbs. Except for this obesity there was nothing significant.

Laboratory Data: The serum cholesterol was 252 mg. per cent, and basal metabolic rates —7. The lowest fasting blood sugar was 41 mg. per cent. A roentgenogram of the skull showed no change in the sella turcica. Electro-encephalograms, interpreted by Dr. Paul Hoefer, showed high voltage, slow activity of irregular pattern while the patient was fasting, and a completely normal pattern within one minute after injection of dextrose during hyperventilation. Five examinations were made in all, and it was the impression that there was a striking relation between electro-encephalogram, clinical picture, and food intake.

Blood sugar during an attack was recorded as 37 mg. per cent. The patient was unconscious. She regained consciousness within two minutes after intravenous administration of 50 cc. of 50 per cent glucose. Attacks occurred almost daily in spite of diet, and often required intravenous glucose for relief. Operation was, therefore, advised, and she was transferred to the Presbyterian Hospital.

Operation.—October 19, 1942: Dr. Fordyce B. St. John and Dr. Allen O. Whipple. The abdomen was explored through a long, curved transverse incision. The pancreas was small. There was a hard nodule palpable in the tail which was thought to be

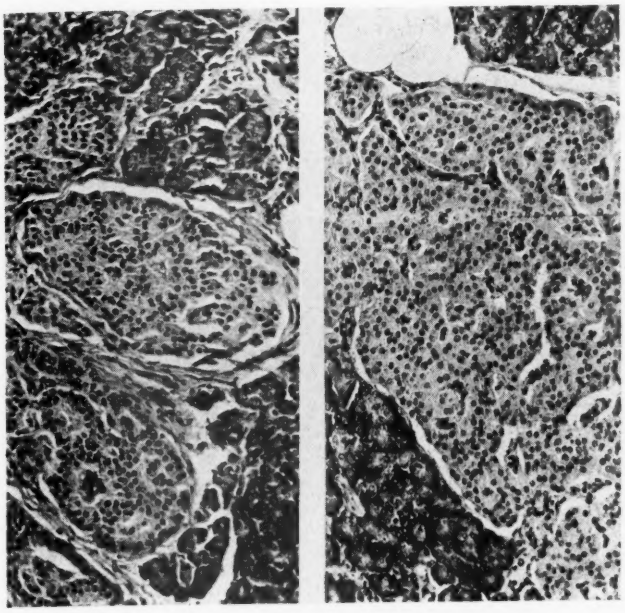

FIG. 3.—Case 1: Higher power photomicrographs showing detail of neoplastic islets.

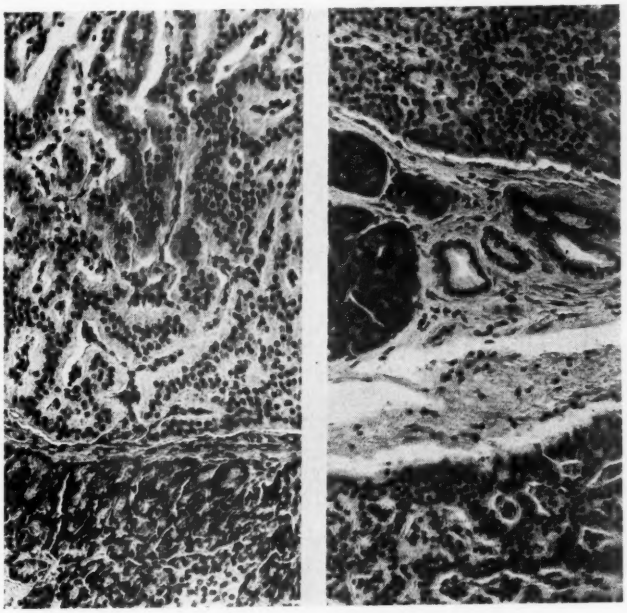

FIG. 4.—Case 2: Comparable fields to Figure 3.

tumor, but satisfactory palpation was difficult because of the patient's obesity. The tail and part of the body were resected. Stubborn bleeding was encountered deep in the left upper quadrant which was controlled by the application of two long, curved clamps, left *in situ*, together with a cigarette drain.

Postoperative Course: The clamps were removed on the seventh postoperative day. The sinus was closed at the end of the fifth week. The patient was discharged on the 47th postoperative day, and the wound was healed in eight weeks.

Subsequent Course: She came for follow-up examination three months after operation, at which time her blood sugar, not fasting, was 103 mg. per cent. Previous fasting blood sugars in the hospital had been as low as 68 mg. per cent on the 46th postoperative day. The patient, however, was on a reducing diet which she continued after leaving the hospital. Six months after operation, April 18, 1944, she again reported at the Follow-up Clinic, free of symptoms of hypoglycemia.

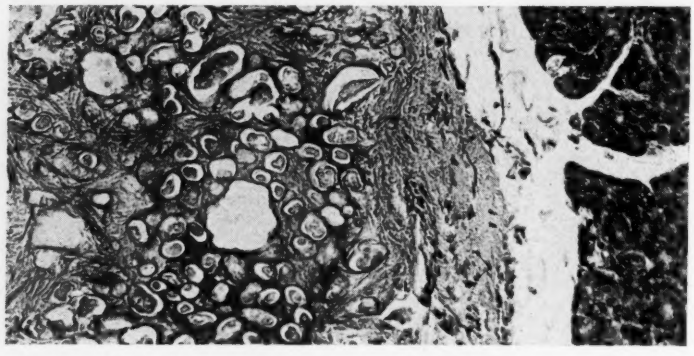

FIG. 5.—Case 2: Typical calcified nodule.

Pathologic Examination.—Gross: S. P. No. 87322. The specimen consisted of a segment of pancreas measuring 5 x 4 x 3 cm., and weighing, fresh, 13 Gm. Attached to the splenic end there was some fat in which there were numerous calcified nodules, 1–2 Mm. in diameter. On section of the pancreas two circumscribed, nonencapsulated, soft, red areas, each about 5 Mm. in diameter, were found. Scattered throughout the rest of the pancreas there were tiny, translucent red areas similar to the two larger ones, and the lesion, after frozen-section at the time of operation, was interpreted as adenomatosis.

Microscopically, on examination of paraffin preparations, this impression was confirmed. Hypertrophy and hyperplasia of islets was seen, and ribbon-like arrangements of islet cells with finger-like extrusions into the adjacent pancreatic tissues. These were typical adenomata. Multiple microscopic areas of calcification were found, interpreted, after considerable study, as calcification of multiple adenomata. The gross calcified masses adjacent to the tail showed tiny remnants of pancreatic tissue also, and were interpreted as larger calcified tumors. (See photomicrographs)

This brings us to the statistical summary of the cases *with tumor,* as we have been able to find them to date (Table I).

In discussing carcinoma of islet cells attention must be drawn to a general article by Duff and Murray (1942), and an excellent review by Hanno and Banks (1943). We have emphasized before the difficulty of being sure of the histogenesis of tumors in which no hypoglycemia is noted. In the

TABLE I

HYPOGLYCEMIA—ISLET CELL TUMORS IN WHICH METASTASES WERE FOUND—FIFTEEN CASES

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TABLE I

HYPOGLYCEMIA—ISLET CELL TUMORS IN WHICH METASTASES WERE FOUND—FIFTEEN CASES

	Author	Date	Sex	Age	Min. Bld. Sugar Mg. %	Operation	Single or Multiple	Result	Autopsy
1	Wilder, Allan, Power, and Robertson	1927	M	40	25	Cholecystectomy. Biopsy of liver	Single	Died one month	Metastases in liver
2	Judd, Faust, and Dixon	1934	F	18	45	Biopsy of metastasis in liver	Single	Died four weeks	Metastases in liver
3	Jacobsen	1934	M	36	25	Biopsy. Tumor size of a grapefruit	Single	Died four months Hemorrhage from duodenum	Extension to duodenum. Metastases in liver
4	Bickel, Mozer, and Junet	1935	M	56	Originally diabetic. Bld. sugar dropped 325—8	None	Single	Autopsy	Metastases in liver, peritoneum, and epicardium. Interstitial pancreatitis
5	Cragg, Power, and Lindem	1937	F	41	30	Biopsy of metastasis in liver	Multiple (diffuse through pancreas)	Died five months	Metastases in liver and lymph nodes. Cysts of ovary
6	Joachim and Banowitch	1938	F	31	30	Resection of spleen and portion of tumor in tail of pancreas and a lymph node showing metastasis. Liver apparently negative	Multiple	Postoperative death	Not done
7	Seckel*	1939	M	36	16	Exploratory	Single	Died ten weeks postoper.	Metastases in liver, one adrenal, spine, lungs, pleura, retroperitoneal and mediastinal nodes
8	Flinn, Beatty, Ginsberg, and Hemsath	1941	F	45	29	None	Single	Autopsy	Metastases in regional nodes and liver. Adrenals enlarged
9	Ballinger (Whipple—Case 18)	1941	M	53	30	Biopsy. Tumor of aberrant pancreas	Single	Died four months postoper. Montefiore Hospital	Extension to liver. Metastases in retroperitoneal nodes, mesentery, lung, adrenals, heart, vena cava, spleen, and subcutaneous tissue of clavicular region
10	Quarrier and Bingham (Case 1)	1942	M	73	21	None	Single	Autopsy	Metastases in liver and regional lymph nodes
11	Gray†	1942	F	48	27	Excision. Tumor in tail	Single	Died six weeks	Metastases in liver. Marked basophilism of pituitary
12	Hanno and Banks	1943	M	68	21	Biopsy of liver metastasis	Single	Died two days	Metastases in liver
13	Holman, Wood, and Stockton (Case 3)	1943	M	45	27	Biopsy of tumor in tail of pancreas and of metastasis in liver	Single	Died 27 days	Metastases in liver. Focal cortical hyperplasia of adrenals
14	Browning	1943	M	36	12	Biopsy of metastasis in liver	Single	Died two months	Metastases in liver and regional nodes
15	Brunschwig, Allen, Owens, and Thornton	1944	M	32	14	1. Sept., '39. Excis. 2 tumors 2. Jan., '40. Excis. large tumor of body and tail 3. Aug., '42. Excis. of most of head. (Liver metastases present) 4. Dec., '43. Pancreaticoduodenectomy. Excis. of liver metastases	Multiple	Died two hours after last operation	Metastases in liver

*Reported also by Brunschwig, Gomori, and Cannon (cited by Gray).
†Reported also by Joslin.

22 cases listed by Hanno and Banks one case is included erroneously (Lloyd). This leaves 21 cases which may be interpreted as malignant. In seven there were no clinical data to establish the diagnosis of hyperinsulinism. (Fabozzi (1903), four cases quoted, considered by many doubtful as to islet cell origin; Zanetti (1927), one case; Hamdi (1932), one case; Evangelisti (1935), one case). In three cases reported by Duff and Murray (1942) hypoglycemia was known to be absent, and the remaining 11 cases, *i.e.*, 11 of 21, were cases of hyperinsulinism, roughly one-half the cases. Our own table lists only 15 cases of carcinoma. These were all cases with hypoglycemia, with metastases, and they include all of the cases of Hanno and Banks in which hypoglycemia was known to be present.*

We have had two cases *without* hypoglycemia, which we have interpreted as islet cell carcinomas.† One was a man, age 69, with extensive liver metastases, found at operation. The pancreas at autopsy proved to be the primary site of tumor, almost six years after the operation, which demonstrated metastatic disease, a longer history than any of the cases *with* hypoglycemia and metastatic disease. The other case is a woman, age 53, who underwent resection of the body and head of the pancreas together with pylorus and duodenum. She has shown no evidence of recurrence to date, four years after operation, and no hypoglycemia.

The cases of hyperinsulinism with islet cell tumor considered benign, removed at operation, we listed in 1940 in Table II. Forty-six cases were listed, one incorrectly, Mathias (see footnote). Of the 45 cases correctly listed five had more than one tumor; Graham and Womack (1933), two tumors; Whipple and Frantz, Case 3 (1935), two tumors; Whipple and Frantz, Case 4 (1935), two tumors; Kalbfleisch, Case 3—Heupke and Obert (1937), five tumors; Frantz, Case 9—Whipple (1940), two tumors. To Table II must be added 31 cases as follows:

The cases of hyperinsulinism with islet cell tumor considered benign found at autopsy we listed in 1940 in Table III. Twenty-four cases were listed, of which three had more than one tumor. (Terbrüggen, Case 1—Frank (1931), multiple; Wolf, Hare, and Riggs (1933), three tumors; Frank, Case 2, (1931), two tumors). To Table III must be added six cases as follows:

The cases of hyperinsulinism with islet cell tumor suspected of being malignant, removed at operation, we listed in 1940 in Table IV. Nineteen cases were listed, of which three had more than one tumor (Judd, Allan, Frank and Rynearson (1933), two tumors; Ziskind and Bayley (1937), two

* There is a sixteenth case of hyperinsulinism, with metastatic islet cell carcinoma, reported by Slye and Wells (1935) but the patient was a dog.

† The difficulties of interpretation are well illustrated by a case with multiple metastases reported by Willis (1936), in which the author is uncertain of the origin; and also by the case of Mathias (1928), which has been repeatedly misquoted, and is wrongly listed in our own report in 1935, where it should appear in Table VII instead of Table III, and again in 1940 where it should not appear in Table II as there was no recorded hypoglycemia.

TABLE II (1940)—Continued

(Ref. Annals of Surgery, 112, No. 2., 167-168, August, 1940)

HYPOGLYCEMIA—ISLET CELL TUMORS REMOVED AT OPERATION. CONSIDERED TO BE BENIGN. TOTAL CASES—SEVENTY-SIX. MULTIPLE TUMORS—ELEVEN

	Author	Date	Single or Multiple
46	Cheley	1934	Single
47	Engel	1934	Single
48	Nesselrode	1934	Single
49	Duncan, Hayward and Fleck (Case 1)	1939	Single
50	Windfild (Case 1)	1940	Single
51	Windfild (Case 2)	1940	2 tumors
52	Windfild (Case 3)	1940	Single
53	Greenlee, Lloyd, Bruecken, and McEllroy	1940	Single (Hyperthyroidism*)
54	Burtness, Koehler, and Saint	1941	Single
55	Magner (Case 1)	1941	Single
56	Meyer, Antman, and Perlman	1941	Single
57	Rudd and Walton	1941	Single (aberrant†)
58	Brown	1942	Single
59	Stein	1942	Single
60	Romano and Coon	1942	Single
61	Erb, Dillon, and Ferguson	1942	Single
62	Thomas	1943	Single (aberrant†)
63	Ceballos and Rosenblatt	1943	Single
64	Spangler	1943	Multiple
65	Holman, Wood, and Stockton (Case 1)	1943	2 tumors (1 aberrant†) Hypertrophy of islets
66	Rayner, Rogerson, and Jones	1943	Multiple
67	Wechsler and Garlock (Case 1)	1944	Single
68	Cole	1944	Single
69	Priestley, Comfort, and Radcliffe	1944	Single (Total pancreatectomy‡)
70	Whipple (Case 11). Not published	1944	Single (reoperation)
71	Whipple (Case 16) Not published	1944	Single
72	Whipple (Case 25) Not published	1944	Adenomatosis
73	Whipple (Case 26) Not published	1944	Single
74	Whipple (Case 27) Not published	1944	Single
75	St. John and Whipple (Case 30) Not published	1944	Adenomatosis
76	Whipple (Case 31) Not published	1944	Single

*The association of thyroid pathology with hypoglycemia has been discussed by John (1931), Aitken (1936), Womack and Cole (1937), and Greenlee, Lloyd, and Bruecken (1940).

†Islet cell tumors of aberrant pancreas have been reported by Vecchi (1914), Stewart and Hartfall (1928), White and Gildea (1937), Rudd and Walton (1941), Ballinger (Whipple—Case 18) (1941), Thomas (1943), and Holman, Wood, and Stockton (1943).

Excision of aberrant pancreatic tissue, not tumor, has been reported by Smith, Frederick G. (1942), and Fanta (1937), both with relief of symptoms. Possible sites of aberrant pancreatic tissue are shown by Faust and Mudgett (1940) in a review of 370 reported cases, and Thorsness (1940).

‡The only other total pancreatectomy recorded is that of Rockey (1943), which was done for carcinoma, *not* islet cell. Survival in this case was only 15 days. In the case of Priestley, Comfort, and Radcliffe (1944), survival has been 16 months, and the resultant diabetes is mild.

TABLE III—Continued

(Ref. ANNALS OF SURGERY, *112*, No. 2., 169, August, 1940)
HYPOGLYCEMIA—ISLET CELL TUMORS FOUND AT AUTOPSY.
CONSIDERED TO BE BENIGN. TOTAL CASES—THIRTY.
MULTIPLE TUMORS—THREE

	Author	Date	Single or Multiple
25	Duncan, Hayward, and Fleck (Case 2)	1939	Single
26	Heyn and Sommer	1940	Single
27	Kerwin	1942	Multiple
28	Quarrier and Bingham (Case 3)	1942	Single
29	Stevenson and Rannie	1942	Single
30	Holman, Wood, and Stockton (Case 2)	1943	Single (aberrant)

TABLE IV—Continued

(Ref. ANNALS OF SURGERY, *112*, No. 2., 170, August, 1940)
HYPOGLYCEMIA—ISLET CELL TUMORS REMOVED AT OPERATION.
SUSPECTED OF BEING MALIGNANT. TOTAL CASES—TWENTY-SIX.
MULTIPLE TUMORS—FOUR

	Author	Date	Single or Multiple
20	Forbes, Davidson, and Duncan	1939	Single
21	Quarrier and Bingham (Case 1)	1942	Single
22	Quarrier and Bingham (Case 4)	1942	Multiple
23	Whipple (Case 20) Not published	1944	Single
24	Whipple (Case 22) Not published	1944	Single
25	Whipple (Case 23) Not published	1944	Single
26	Whipple (Case 29) Not published	1944	Single

TABLE V—Continued

(Ref. ANNALS OF SURGERY, *112*, No. 2., 171, August, 1940)
HYPOGLYCEMIA—ISLET CELL TUMORS FOUND AT AUTOPSY.
SUSPECTED OF BEING MALIGNANT. TOTAL CASES—TWO (NO NEW CASES).
MULTIPLE TUMORS—NONE

tumors; J. Smith (1939), multiple). To Table IV must be added seven cases as follows:

Two cases of hypoglycemia with islet cell tumors suspected of being malignant, found at autopsy listed in 1940 in Table V. Both were single. We have found no new cases of this sort reported at autopsy since then.

It will be noted that of tumors considered benign 14.2 per cent were multiple; of suspicious tumors, 14.3 per cent; and of tumors of proven malignancy, 20 per cent. We must emphasize again that in the group of suspicious tumors *the suspicion, of the pathologist not the surgeon, has yet to be confirmed in a single case by follow-up data.*

To the cases of multiple tumor and of true adenomatosis there must be added for completeness those cases with hypoglycemia in which, in the pathologist's opinion, although there was no true neoplasia, there was hypertrophy and hyperplasia. There are 11 such cases, and Table VI, therefore, is an analysis of the whole group.

Summarized, all of the foregoing figures give us totals seen in Table VII.

TABLE VII

SUMMARY OF STATISTICS

	Single	Multiple	Total	Per Cent Multiple
Tumors removed at operation and considered benign	65	11	76	
Tumors found at autopsy and considered benign	26	4	30	
Total benign tumors	91	15	106	14.2
Tumors removed at operation and suspected malignant	22	4	26	
Tumors found at autopsy and suspected malignant	2	0	2	
Total suspicious tumors	24	4	28	14.3
Total cases of tumor *without proven malignancy*	115	19	134	14.2
Carcinoma with metastases, *proven malignancy*	12	3	15	20.0
TOTAL CASES OF TRUE NEOPLASM	127	22	149	14.8
HYPERTROPHY AND HYPERPLASIA WITHOUT NEOPLASM			11	

SUMMARY

The review of published cases and those in our own series, presented in 1940, is here extended to include the rest of the cases in the literature, as we have been able to find them, and the new cases in our own series.

Two of our own cases are analysed in detail as they are the first in which a diagnosis of hyperinsulinism with adenomatosis has been made.

CONCLUSIONS

Multicentric origin of benign and malignant tumors of islet cells is suggested by the pathologic findings in the cases reviewed.

In the multicentric cases with hyperinsulinism there seems to be a good possibility that hyperplasia and neoplasia in the remaining pancreas may result in return of hypoglycemic symptoms.

In the multicentric cases the possibility of malignant disease must be considered.

Such cases should be followed for long periods in order to establish a basis for prognosis in others.

TABLE VI

HYPOGLYCEMIA—HYPERTROPHY, HYPERPLASIA, MULTIPLE TUMORS, AND ADENOMATOSIS

	Author	Date	Sex	Age	Min. Bld. Sugar Mg. %	Operation or Autopsy	Pathology	Result
1	Massa	1929	M	67	58	Autopsy	Hypertrophy of islets. Adenocarcinoma of pancreas with obstruction of ducts and metastases	Autopsy
2	Terbruggen	1931	F	30	23	Autopsy	Five tumors encapsulated, and many tiny ones. Islets normal. Adenomatosis?	Autopsy
3	Phillips	1931	M	56	25	Autopsy	Hypertrophy of islets	Autopsy
4	Graham and Womack	1933	M	22	25	1. Excis. of tumor. 2. 4 cm. of tail excised	1. Adenoma 1 x 0.8 cm. 2. Adenoma 2 cm.	1. No improvement 2. Symptoms relieved. Mental deterioration
5	Mosenthal and MacBrayer... (Quoted by Wilder)	1933	M	39	50	Autopsy	Hypertrophy of islets	Autopsy
6	Wolf, Hare, and Riggs	1933	M	10	54	Autopsy	Three tumors, middle, tail, and head. 1, 0.3, 0.3 cm.	Autopsy
7	Judd, Allan, Frank and Rynearson (Case 7)	1933	M	32	40	Two tumors, 1.5 cm. and 2 cm., respectively	Carcinoma?	Symptom-free 23 months
8	Simon	1934	M	26	51	Resection 60 Gm.	Hypertrophy of islets	Improved 2 months
9	Frank (Case 2)	1935	F	14	11	Autopsy	Two tumors, head and tail	Autopsy
10	Dannenberg, Bell and Gouley.	1935	M	3	71	Autopsy	Hypertrophy and hyperplasia of islets. Fibrosis of pancreas	Autopsy
11	Whipple and Frantz (Case 3)	1935	M	28	38	1. Excis. tumor junction body and tail 2. Excis. tumor tail	1. Adenoma 2. Adenoma	Symptom-free. Died duodenal hemorrhage 18 months
12	Whipple and Frantz (Case 4)	1935	M	38	30	Excis. tumors—1 cm. in body, 0.6 cm. in head	Adenomas	Symptom-free 105 months
13	McCaughan and Broun (Case 1)	1937	M	20	54	Resection of tail 8 Gm.	Number of islets increased	Some improvement
14	McCaughan and Broun (Case 2)	1937	M	17	36	Resection — body and tail (22.5 Gm.)	Hypertrophy of islets	No improvement
15	McCaughan and Broun (Case 6)	1937	F	24	70	Resection 35 Gm.	Hypertrophy of islets	No improvement

16	Kalbfleisch..... (Neupke and Obert—Case 3)	1937	M	23	20	Excis. tumor of body	Adenoma	Died two days postoper. Four of five tumors found at autopsy. Adenoma of hypophysis and of parathyroid. Hyperplasia of thymus
17	Ziskind, Bayley, and Mauer...	1937	F	19	40	Explor. No tumor. Reoper. P.P. two tumors in body	Carcinoma?	Died 32 hours postoper. Third tumor in remaining body. No metastases
18	Brinck and Sponholz.....:	1938	F	49	59	Autopsy	Hyperplasia of islets. Pancreaticolithiasis	Autopsy
19	Smith, Joseph.....:....	1939	F	35	31	Resection (22 Gm.)	Multiple nodules. Incomplete capsules. Carcinoma?	Symptom-free five months
20	Frantz.....:.. (Whipple—Case 9)	1940	F	45	26	1. Subtotal pancreatectomy; tumor 0.4 mm. in tail 2. Excision tumor in head	1. Adenoma 2. Adenoma	Not improved
21	Winfild..... (Case 2)	1940	M	22	37	Resection	Two tumors 2 cm. apart. Each 0.5 cm. in diameter	Slight hypoglycemic attacks — six months
22	Magner..... (Case 2)	1941	F	20	55	Resection of body and tail	Diffuse hypertrophy and hyperplasia	Symptom-free two years
23	Kerwin.....	1942	F	42	43	None. Autopsy	Two tumors	Autopsy
24	Quarrier and Bingham.....	1942	F	20	23	Excision tumors of pancreas and adrenal	Three islet cell tumors. Carcinoma? Adrenal carcinoma	Died postoper.
25	Spangler.....	1943	M	26	32	Excision of tumors	Three adenomas. (Bilateral urinary calculi)	Symptom-free three weeks
26	Holman, Wood, and Stockton (Case 1)	1943	F	Adult	37	1. Partial pancreatectomy 2. Excision of aberrant tumor	1. Adenoma and hypertrophy of islets 2. Adenoma	Symptom-free one year
27	Rayner, Rogerson, and Jones.	1943	F	46	21	1. Resection (36 Gm.) 2. Excision of tumors in head	1. No tumor 2. Three small, round tumors grouped together	1. Symptoms continued 2. Relief of symptoms
28	Whipple..... (Case 21). Not published	1944	M	50	36	Resection (38 Gm.)	Hyperplasia	Unimproved. Suicide two months postoper.
29	Whipple..... (Case 25). Not published	1944	F	46	23	1. Excision of tumor (MacDonald) 2. Excision of tumor (MacDonald) 3. Resection (8 Gm.) (Whipple)	1. Adenoma 0.5 cm. 2. Adenoma 0.75 cm. 3. Adenomatosis	Symptom-free 16 months
30	St. John-Whipple.....: (Case 30). Not published	1944	F	32	41	Resection (13 Gm.)	Adenomatosis	Symptom-free six months

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PANCREATICOJEJUNOSTOMY AND OTHER PROBLEMS ASSOCIATED WITH THE SURGICAL MANAGEMENT OF CARCINOMA INVOLVING THE HEAD OF THE PANCREAS

REPORT OF FIVE ADDITIONAL CASES OF RADICAL PANCREATICODUODENECTOMY

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IT has become increasingly apparent during the past five years or so that surgical armamentaria have been increased to a point where carcinoma involving the head of the pancreas may be attacked radically. It is common knowledge that prior to 1935 sporadic attacks were made upon cancer in this region. The incidence of success, however, was so meager and the mortality so high that no operation contemplating eradication of the disease ever gained any degree of popularity. The most complete review of these early experiences may be found in Hunt's[1] review of the subject, appearing in 1941.

Largely due to the impetus given this problem by Whipple, Parsons and Mullins,[2] in 1935, and by Whipple,[3] in 1938, the entire subject has been reopened and the number of successful attacks upon ampullary and periampullary carcinomata have been increasing yearly.[3–12] In order to further the study of patients confronted with cancer in this region and to counter the all too generally held impression that its surgical attack is hopeless, the following seven cases are recorded. In general, these experiences parallel those reported from other institutions with regard to mortality, postoperative complications and the evolution of the operation as it is now commonly performed.

One of these cases (Case 4) has been previously reported[9] but is included here for the sake of completeness. The significant features of each case are recorded in Table I, while more detailed clinical abstracts appear in the case reports.

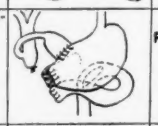
In view of the fact that each of these cases demonstrates one or another of the significant phases in the evolution of this major surgical operation they may best be discussed under subject headings rather than as individual cases.

Diagnosis.—One of the most difficult problems associated with the surgical management of these patients is the establishment at the operating table of a positive diagnosis of cancer. In this respect these tumors may be conveniently divided into two groups: Those in and about the ampulla of Vater, and those lying deeply in the head of the pancreas. The former usually offer no great difficulty save for the fact that upon frozen section of their more or less superficial portions these polypoid tumors may appear

benign under the microscope, where actually they are malignant. If, however, it is borne in mind that very few ampullary tumors are benign, it is obvious that unless their benignity can be clearly demonstrated, they should, if possible, be subjected to radical removal. Case 6 is an excellent example of this problem. Numerous frozen sections at the first operation all showed a benign tumor, and it was upon this assumption that local excision was per-

TABLE I

SIGNIFICANT FEATURES OF SIX CASES OF RADICAL PANCREATICODUODENECTOMY

PATIENT NO. AGE SEX	HISTORY AND PHYSICAL EXAMINATION	DIAGNOSIS	OPERATION	OPERATION DIAGRAMMED	P.O COMPLICATIONS	FOLLOW-UP
CASE 1. R.A NO. 277074 57YRS. M	ABDOMINAL DISTRESS 3 WKS. JAUNDICE 2 WKS WT. LOSS 10 LBS P.E JAUNDICED	CARCINOMA OF AMPULLA OF VATER	1. GASTROENTEROSTOMY CHOLECYSTGASTROSTOMY 2. TRANSDUODENAL EXCISION REIMPLANTATION OF COMMON AND PANCREATIC DUCTS		NONE	WELL 2 YRS. RECURRENCE. 3 YEARS
CASE 2. F.B. NO. 276140 56YRS. F	LOSS OF APPETITE 2 1/2MS. MILD JAUNDICE 2 MOS. DEEP JAUNDICE 1 WK NO WEIGHT LOSS P.E. NEGATIVE	CARCINOMA OF AMPULLA OF VATER	1. DUODENOSTOMY, GASTROENTEROSTOMY, LIGATION COMMON DUCT CHOLECYSTGASTROSTOMY 2. PANCREATICODUODENECTOMY 3. ATTEMPTED CLOSURE DUODENAL STUMP 4. JEJUNOSTOMY		PERSISTENT COMPLETE DUODENAL FISTULA	P.O. DEATH
CASE 3. P. D. M. NO. 254422 52YRS. M	PAINLESS PROGRESSIVE JAUNDICE 4 MOS. WEIGHT LOSS 30 LBS P.E. LARGE PALPABLE GALL BLADDER	CARCINOMA OF PANCREAS	1. CHOLECYSTGASTROSTOMY GASTROENTEROSTOMY 2. PANCREATICO-DUODENECTOMY 3. RESECTION OF FISTULOUS TRACT		PERSISTENT PANCREATIC FISTULA SEVERE STEATORRHEA	LIVED 8 MONTHS (NO POST-MORTEM)
CASE 4. J.B NO. 311583 57YRS M. PREVIOUSLY REPORTED	PAINLESS JAUNDICE 1 MON. WEIGHT LOSS 20 LBS. P.E JAUNDICED	CARCINOMA OF DUODENUM	RADICAL PARTIAL PANCREATECTOMY DUODENECTOMY PANCREATICOJEJUNOSTOMY CHOLECYST JEJUNOSTOMY GASTRO JEJUNOSTOMY		P.O PNEUMONIA INTERMITTENT ATTACKS CHOLANGITIS	LIVED 14 MONTHS DIED OF CARCINOMATOSIS POST MORTEM
CASE 5. N. M NO. 361219 69YRS. M	PAINLESS JAUNDICE 6 WKS WEIGHT LOSS 30 LBS. P.E. JAUNDICED	CARCINOMA OF AMPULLA OF VATER	RADICAL PARTIAL PANCREATECTOMY DUODENECTOMY PANCREATICO JEJUNOSTOMY CHOLECYST JEJUNOSTOMY GASTROJEJUNOSTOMY		P.O WOUND INFECTION	WELL 1 YEAR
CASE 6. S.H NO. 363096 55YRS. F	PAINLESS JAUNDICE, INTERMITTENT 5 WKS. NO WEIGHT LOSS P.E. JAUNDICE	CARCINOMA OF AMPULLA OF VATER	1ST. ADMISSION EXCISION AMPULLARY CARCINOMA 2ND. ADMISSION 2 MOS. LATER RADICAL PANCREATICODUODENECTOMY PANCREATICO JEJUNOSTOMY CHOLEDOCHOJEJUNOSTOMY GASTRO JEJUNOSTOMY		NONE	WELL 3 MONTHS
CASE 7. W.M. NO. 375853 67YRS M	EPIGASTRIC FULNESS 2 MOS. WEIGHT LOSS 20 LBS. P.E. EPIGAST. TUMOR	CARCINOMA OF STOMACH WITH EXTENSIONS TO HEAD OF PANCREAS	SUBTOTAL GASTRIC RESECTION PARTIAL PANCREATIC RESECTION DUODENECTOMY PANCREATICO JEJUNOSTOMY CHOLEDOCHOJEJUNOSTOMY GASTRO JEJUNOSTOMY		NONE	WELL 2 MONTHS

formed. Following removal, however, a section from the base of the tumor was obviously malignant.

The second group, those primary in the head of the pancreas, may offer great difficulty in clearly establishing their malignant nature at the operating table. This, of course, is due to the fact that not infrequently these tumors have their origin deep in the gland itself and, as they grow, they continue

to be surrounded by a shell of pancreatic tissue. And it is only this normal tissue that is generally accessible for frozen section. Further confusion in this regard may also arise from the fact that since these lesions frequently obstruct one or more branches of the duct system of the pancreas, the gross and microscopic picture of chronic pancreatitis is presented. Because the most difficult differential diagnosis lies between this entity and carcinoma, the problems associated with the accurate diagnosis of these lesions can readily be appreciated. This dilemma has led Cattell[10] to point out that frequently the decision as to whether or not to perform a radical operation must depend upon the surgeon's ability to make a diagnosis based upon the clinical and gross pathologic findings. This, of course, may, at best, be uncertain, and undoubtedly will mean that as more and more of these tumors are attacked surgically, some patients will undergo a radical procedure for chronic pancreatitis. At the moment, there is not apparent any exact solution of this problem. The most logical approach, however, would seem to be one of carefully weighing all the details of a given case, and proceeding upon what seems to be the most reasonable course.

In connection with this problem of diagnosis a related situation may be mentioned. In patients requiring common duct exploration in which an associated chronic pancreatitis is found, it may be wise to leave a small catheter in the common duct in order to obtain postoperative choledochograms. If such roentgenologic studies demonstrate a persistent obstruction of the common duct not due to overlooked stones, a number of pancreatic carcinomata will undoubtedly be discovered sufficiently early to warrant re-exploration at a time when such a tumor may be amenable to radical extirpation.

Local Excision of Ampullary Tumors.—Because local excision of small ampullary tumors, together with reimplantation of the common and pancreatic ducts, is a relatively innocuous procedure, the early literature upon this subject is replete with case reports of transduodenal excision of these carcinomata.

A critical review of 98 patients subjected to this operation, as compiled by Hunt,[1] reveals that the postoperative mortality was 27 per cent, and that but five patients were alive over four years. Three of these may be considered cured, as they were well five, nine, and 22 years after operation. These data indicate that local excision of these tumors may be expected to yield an occasional long-range cure, but that certainly the incidence is low.

In this series, there are two cases in point (Cases 1 and 6). In Case 1 there was an apparent cure for three years but at the present time the patient presents complaints suggestive of recurrence. Case 6 promptly recurred after local excision.

One- Versus Two-Stage Operation.—Whipple's[2] original communication postulated a two-stage operation. The many disadvantages attendant upon this soon became evident. With the discovery of the ability to control the

bleeding tendency in jaundiced patients by means of vitamin K, one of the foremost reasons for the two-stage procedure became invalid, and, in 1940, Whipple[11] performed, for the first time, the operation of radical pancreaticoduodenectomy in one stage. Since then the operation of choice has been that of complete extirpation of the pancreatic head and duodenum at one sitting, reserving the two-stage procedure only for the poorest of operative risks.

Extent of Duodenum to Be Removed.—One of the most dreaded complications of operative procedures involving the duodenum is that of fistula formation at the site of closure of the duodenal stump. Early in the history of the development of the two-stage operation only that portion of the duodenum adjacent to the head of the pancreas was removed. Because this may leave the blood supply of the remainder of the duodenum seriously impaired, it is considered necessary to remove all of this structure together with the upper few centimeters of the jejunum. Case 2 is one in which a persistent duodenal fistula, which defied closure, undoubtedly was the greatest single factor contributing to her death.

Cholecystenterostomy versus Choledocho-enterostomy. — The problem whether to secure external drainage of the biliary tract by way of the gallbladder or the common duct has been much discussed. In the two-stage operation it would have been obviously disadvantageous to have obscured the operative field by some form of choledochojejunostomy; therefore, the gallbladder had of necessity to be used, the anastomosis usually being performed between this organ and the stomach. This, all too frequently, presented two untoward complications; early, that of a biliary fistula at the site of division of the common duct; late, of an ascending biliary tract infection. With the acceptance of the one-stage procedure the possibility of the development of both of these sequelae could be minimized by the performance of a choledochojejunostomy. Although the gallbladder was utilized in Cases 2, 3, 4 and 5 without the development of any immediate postoperative complication, troublesome attacks of acute cholangitis marred the result in Case 4. In Cases 6 and 7 the common duct was employed at the suggestion of Doctor Whipple (Discussion[9]). In neither of these cases has any untoward complication developed. In the future it will undoubtedly be the policy of this clinic to utilize the common duct whenever possible.

Management of the Pancreatic Stump.—The best method of dealing with the pancreatic stump has proved a troublesome problem centering about two controversial points: First, whether or not the external pancreatic secretion is necessary for the maintenance of an adequate digestive process, particularly of fats. It is unquestioned that an, as yet, undetermined percentage of patients tolerate deprivation of their external pancreatic secretions reasonably well. There are a number, however, of which Case 3 is an example, who persistently suffer from a severe degree of steatorrhea following ligation of their pancreatic ducts. The significant single fact is that it cannot be forecast prior to operation to which group any given patient will ultimately

belong. It would seem apparent, therefore, that until further information is available the external pancreatic function should, if possible, be maintained.

The second difficulty lies in the fact that no matter how meticulously the pancreatic duct and stump are closed, there is the risk of the formation of a postoperative fistula. This undesirable, and oftentimes fatal, compli-

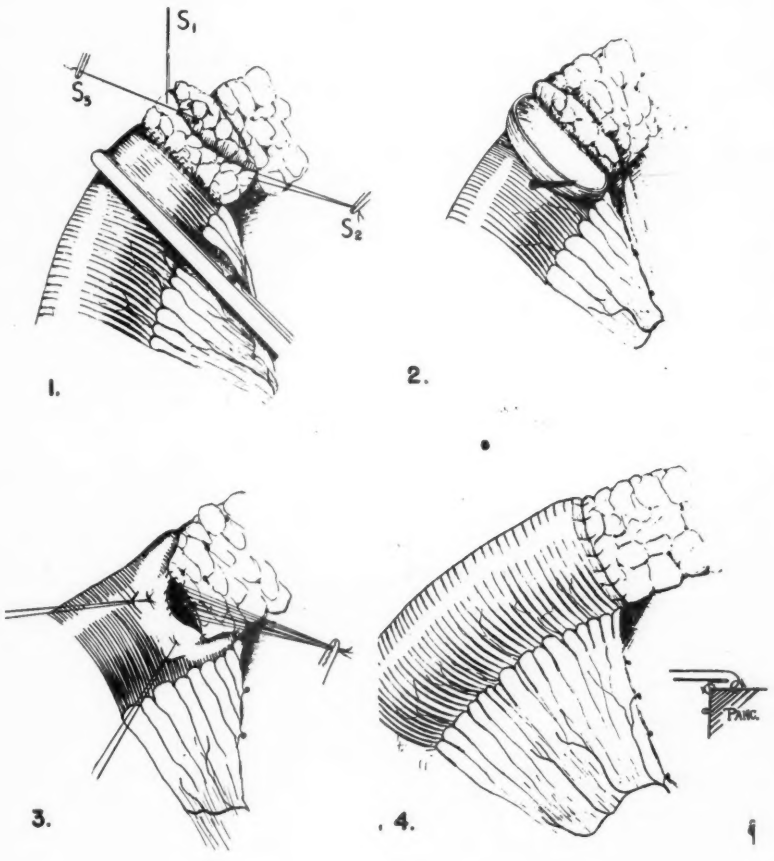


FIG. 1.—(1) First suture line in place, approximating the posterior aspect of the pancreas and the jejunal wall. (2) Second posterior suture line, approximating the posterior cut-surfaces of the pancreas and jejunum. (3) First anterior suture line, placed but not completed. Just before these last few are tied, the ligature is removed from the pancreatic duct, permitting its immediate drainage into the jejunum. (4) Completed anastomosis. The inset demonstrates that the pancreatic stump is actually introduced into the inverted end of the jejunum.

cation may be avoided by a safe method of anastomosis between the intestinal tract and pancreatic stump. That such a satisfactory method is available seems apparent from examination of Cases 4, 5, 6 and 7, in which drainage of the external pancreatic secretions into the gastro-intestinal tract was secured by suture of the proximal end of the pancreas into the open end of the jejunum. The method by which this has been accomplished is outlined in some detail as follows:

Method of End-to-End Pancreaticojejunostomy.—After completion of the radical removal of the duodenum and head of the pancreas, the proximal end of the jejunum is passed to the upper abdomen through a suitable rent in the mesocolon. As shown in Figure 1, the posterior aspect of the distal two centimeters of the pancreas is freed from the underlying tissues and held with its cut-surface upward by two suitably placed silk stay-sutures S. 1 and S. 2. Additional traction may be secured if necessary by means of S. 3, the silk ligature placed upon the dilated pancreatic duct as it was divided earlier in the course of the operation. Traction sutures are to be preferred to hemostats or Allis clamps because they are far less damaging to the friable pancreatic tissue. The jejunum is approximated to the posterior aspect of the pancreas by means of a suture line composed of interrupted fine silk sutures placed as shown (Fig. 1 (1)). These are placed deeply in the substance of the gland, include the jejunal submucosa, and are tied loosely in order to avoid jeopardizing the blood supply of the included tissues.

As shown in Figure 1 (2), the clamp upon the jejunum is next removed, its bite of necrotic tissue carefully excised, and the posterior cut-border of the pancreatic stump approximated to the adjacent jejunal mucous membrane, again, with interrupted sutures of fine silk. Similarly, the anterior cut-borders of the pancreas and jejunum are approximated as shown in Figure 1 (3). Just prior to the completion of this third row of sutures the fine silk ligature securing the pancreatic duct is removed, establishing immediate drainage into the lumen of the jejunum. By gentle manipulation the stump of the pancreas is then actually introduced into the inverted end of the jejunum. This inversion is then maintained by a fourth row of interrupted fine silk sutures, comparable to the first row, as shown diagrammatically in Figure 1 (4).

Brunschwig[8] has recently raised the question "of whether appreciable pancreatic secretion may obtain after such implantations." That appreciable amounts of pancreatic secretion do gain entrance to the gastro-intestinal tract following this procedure is indicated, first, by the experimental studies of Person and Glenn,[14] in which a perfectly functioning pancreaticogastrostomy was demonstrated following implantation of the stump into the posterior wall of the stomach; second, by Case 4, in which the presence of pancreatic enzymes was demonstrated in the intestinal tract by means of the secretin test; third, by Cases 4, 5, 6 and 7, in which there has been no evidence of digestive disturbances following operation. In these four cases there has been no instance of the development of a postoperative pancreatic fistula, a most undesirable complication not only from the point of view of the difficulty involved in the management of the fistula itself, but also because of the danger of severe hemorrhage associated with the escape of pancreatic juice into the site of a but recently completed operation.

Gastrojejunostomy.—Judging from the reported cases and from this series, much latitude may be exercised in reestablishing the continuity of the

stomach and jejunum. As a matter of principle a stoma so placed as to prevent the enteric stream from passing either the pancreatic or biliary anastomosis is to be preferred. In Case 4 it is noted that the cholecystojejunostomy lay distal to the gastro-enterostomy. This may well have been a factor contributing to this man's episodes of biliary tract infection. At the present time an effort is made to place the gastro-enterostomy as illustrated in Cases 5, 6 and 7. Whether ante- or retrocolic would appear to be of minor significance.

Suture Material.—Throughout all of these radical procedures silk has been used entirely except for the mucosal suture in the biliary and gastric anastomoses. Particularly is the use of silk important in performing not only the pancreatic anastomosis but also in securing hemostasis, for catgut is digested with amazing rapidity by pancreatic juice. It is probable that much of the current pessimism expressed toward pancreatico-enterostomies finds origin in the poor results obtained at a time when catgut was used almost exclusively.

Closure of the Abdominal Wall.—In this entire series, with the exception of the last case, all of the abdominal wounds were closed with through-and-through silver wire stay-sutures together with catgut approximating the individual layers.[13] Although several of these individuals developed rather severe wound infections there was no case in which wound disruption or evisceration occurred. The last case was closed with buried double medium silk securing all layers with a modified on-end mattress suture. The significant factor in wound closure in these patients is considered to be the inclusion of some form of nonabsorbable suture that will permit adequate wound drainage, without the risk of disruption should infection occur.

Drainage.—It is important to secure drainage of the site of the pancreatic anastomosis. This is performed by preference through a stab wound in the flank, placing the drains to the neighborhood of, though not actually to, the pancreaticojejunostomy suture line. This suture line incidentally can usually be reasonably well protected by an adjacent tab of omental or retroperitoneal fat.

Anesthesia.—Open-drop ether was employed with satisfaction in all of these patients save the last (Case 4) in which continuous spinal was administered. Because of the many advantages associated with the latter agent, it may become the anesthesia of choice in the future.

CLINICAL ABSTRACTS OF CASE REPORTS

Case 1.—N. Y. H. No. 277074: R. A., age 57, male.

Diagnosis: Carcinoma of ampulla of Vater.

History: This 57-year-old white male gave a history on admission of vague upper abdominal distress of three weeks' duration, associated with the onset of jaundice a week later, and a weight loss of ten pounds.

Physical Examination: Revealed a poorly nourished man, moderately jaundiced. On abdominal examination the liver edge was palpable 4 cm. below the right costal margin.

Laboratory: The only significant finding was the presence of bile in the urine. The stools were light brown and negative for blood.

Roentgenology: Negative G. I. series.

Operations: First—September 17, 1940. Exploratory celiotomy led to the discovery of a movable tumor of the ampulla of Vater. A posterior gastro-enterostomy and a cholecystogastrostomy were performed as a first-stage Whipple procedure.

Second—September 30, 1940. Transduodenal local excision of a carcinoma of the ampulla of Vater, with implantation of the common and pancreatic ducts. Because of the small size of the ampullary tumor it was not considered necessary to subject this patient to the hazards of the second-stage Whipple operation, *i.e.*, radical pancreatico-duodenectomy.

Follow-up: 1 year —Well. Back at work. No complaints.
2 years—Well. Back at work. No complaints.
3 years—Well. Back at work. No complaints.
3.5 years—Patient beginning to complain of loss of appetite and of weight, together with upper abdominal pain. Physical examination negative. A definite diagnosis of recurrence cannot be made at this time, but in view of the patient's difficulties it seems probable.

Case 2.—N. Y. H. No. 276140: F. B., age 56, female.

Diagnosis: Carcinoma of ampulla.

History: Mother and one brother died of carcinoma.

This 56-year-old housewife gave a history of progressive loss of appetite of two and one-half months, and of mild jaundice and pruritis of two months. She became deeply jaundiced one week before admission. No weight loss.

Physical Examination: This revealed an obese white female who was deeply jaundiced. On abdominal examination the liver was palpable one centimeter below the right costal margin.

Laboratory: The significant finding was a positive reaction for blood in the stools.

Roentgenology: Negative G. I. series.

Operations: First—September 9, 1940. Duodenotomy and biopsy of ampullary tumor. Ligation of common duct. Posterior gastrojejunostomy. Cholecystogastrostomy.

Postoperative Course: Unremarkable. Icteric index became normal.

Second—October 15, 1940. Partial resection of duodenum and head of the pancreas. Closure of duodenal and pancreatic stumps.

Postoperative Course: Developed a duodenal fistula, draining as much as 5000 cc. a day.

Third—October 31, 1940. Unsuccessful attempt to close the duodenal stump.

Postoperative Course: Persistent duodenal fistula.

Fourth—November 15, 1940. Jejunostomy for enteric feeding.

November 29, 1940.—Postoperative death due to inanition and sepsis.

Postmortem Examination: Duodenal fistula and localized abscess.

Case 3.—N. Y. H. No. 254422: P. DiM., age 52, male.

Diagnosis: Carcinoma of head of the pancreas.

History: This 52-year-old white male gave a history of progressive painless jaundice of four months' duration, associated with a weight loss of 30 pounds.

Physical Examination: Revealed a deeply jaundiced white male, with an enlarged, easily palpable, nontender gallbladder.

Laboratory: The stools were negative for blood. The prothrombin was 48 per cent, rising to 70 per cent after administration of vitamin K.

Roentgenology: G. I. series revealed a mucosal irregularity in the second portion of the duodenum.

Operations: First—January 15, 1940. Cholecystogastrostomy and posterior gastro-enterostomy.

Second—February 1, 1940. Resection of pancreatic head and first and second portions of duodenum. Closure of the pancreatic stump.

Postoperative Course: Patient developed both a pancreatic and biliary fistula which closed spontaneously after five months, only to break open again within one week. An attempt to resect and reimplant the fistulous tract was unsuccessful, and the patient finally died after eight months of all but continuous hospitalization. During the entire postoperative period he was unable to digest fat, as manifested by persistent steatorrhea.

Case 4.—N. Y. H. No. 311583: J. B., age 57, male. (Previously reported[8]).

Diagnosis: Carcinoma of duodenum.

History: This 57-year-old white male presented himself complaining of jaundice, cutaneous pruritis, and a weight loss of 20 pounds over a course of one month.

Physical Examination: Revealed a well-developed and well-nourished jaundiced male. On abdominal examination the liver edge could be felt 3 cm. below the right costal margin, and the gallbladder was easily felt.

Laboratory: Hb. 10 Gm. R. B. C. 3.8 M. W. B. C. 9,050. Urine: Bile present. Stools positive for blood. Prothrombin time 61 per cent rising to 100 after vitamin K.

Roentgenology: G. I. series revealed marked irregularity of the mucosal pattern in second and third portions of the duodenum.

Operation: November 28, 1941. Radical partial pancreatectomy and duodenectomy. The enteric canal was reestablished first, by retrocolic pancreaticojejunostomy, then an antecolic gastrojejunostomy and, lastly, an antecolic cholecystojejunostomy. The right gutter was drained through a stab wound in the flank.

Postoperative Course: Patient developed an atelectasis followed by pneumonia. He was discharged well 30 days after operation.

During the next 12 months the patient was readmitted twice because of rather severe attacks of acute cholangitis. Fourteen months after his initial operation he was readmitted because of reappearance of his jaundice. Exploratory celiotomy revealed extensive intra-abdominal carcinomatosis; the patient died several weeks later. At postmortem examination an effort to examine the pancreaticojejunostomy was unsuccessful because of massive replacement with tumor.

Case 5.—N. Y. H. No. 361219: W. M., age 69, male.

Diagnosis: Carcinoma of ampulla of Vater.

History: This 69-year-old white male presented himself with a history of the sudden onset of jaundice six weeks prior to admission. As the jaundice increased he lost his appetite and 30 pounds in weight.

Physical Examination: Revealed an intensely jaundiced, somewhat senile male in no acute distress. B. P. 175/90. Examination of the abdomen revealed a liver palpable 3–4 cm. below the right costal margin.

Laboratory: Urine: Bile present. Stools positive for blood. Prothrombin 45 per cent rising to 80 per cent after vitamin K.

Operation: July 3, 1943. Resection of the head of the pancreas and duodenum. In succession, a retrocolic anastomosis was performed between the pancreas and jejunum, end-to-end, between the gallbladder and jejunum, side-to-side, and between the open end of the stomach and the side of the jejunum.

Postoperative Course: This was complicated by extensive suppuration of the abdominal wound. This subsided under adequate therapy, and the patient was discharged well on the 42nd day after operation.

Follow-up: Gained 30 pounds. No digestive disturbance. Entirely well one year after operation.

Case 6.—N. Y. H. No. 363096: S. H., age 55, female.

Diagnosis: Carcinoma of ampulla of Vater.

First Admission. History: This 55-year-old Italian female gave a history on admission of intermittent painless jaundice of five weeks' duration. No loss of appetite. No weight loss.

Physical Examination: Revealed a well-developed and well-nourished woman who was moderately jaundiced. B. P. 150/70. Abdomen: No masses or solid viscera palpable.

Laboratory: Urine strongly positive for bile. Serum proteins 4.8 Gm./100 cc. Stools positive for blood. Hb. 12.2 Gm. R. B. C. 3.8 M. W. B. C. 14,000. Prothrombin 78 per cent rising to 92 per cent after vitamin K.

Preoperative Care: Three transfusions.

Operation: August 17, 1943. At exploration of the ampulla through a duodenotomy, a small soft adenomatous tumor was found which did not appear malignant either in the gross or upon frozen-section. Accordingly, a presumabily complete local excision was performed transduodenally and the common and pancreatic ducts reimplanted.

Postoperative Course: Her jaundice cleared rapidly and she was discharged well on her 18th postoperative day.

Second Admission. Within three weeks after discharge she again became jaundiced, and was readmitted to the hospital.

Physical Examination. On this admission an enlarged gallbladder was easily palpable.

Laboratory: Icteric index 152.

Second Operation: December 20, 1943, two months after local excision. At exploration a firm tumor mass occupying the head of the pancreas was discovered. In spite of the numerous adhesions due to the previous operation the lesion could be easily mobilized and was subjected to radical pancreaticoduodenectomy in one stage. In succession, the following retrocolic anastomoses were performed: Pancreas and open end of jejunum, choledochus and jejunum, end-to-side, and stomach to jejunum, end-to-side. A small tube was placed in the gallbladder as a safety valve for the biliary tract.

The postoperative course was unremarkable. The patient was discharged on her 21st postoperative day.

Case 7.—N. Y. H. No. 375553: W. H. J. M., age 65, male.

Diagnosis: Carcinoma of stomach invading head of the pancreas.

History: On admission the patient's complaint was one of persistent epigastric fullness after ingestion, even of liquids, for the previous two months.

Physical Examination: Poorly nourished white male in no distress. B. P. 150/98. On examination of the abdomen a hard, freely movable mass could be felt in the right upper quadrant.

Laboratory: Urine 2 plus sugar. Fasting blood sugar 150 mg./100 cc. Hb. 80 per cent. R. B. C. 4.5 M. W. B. C. 7,800. Plasma proteins 6.5 Gm./100 cc. Stool repeatedly positive for blood.

Roentgenology: G. I. series led to a diagnosis of carcinoma of the pyloric end of the stomach with 75 per cent retention at six hours.

Operation: January 6, 1944. On exploration an obvious carcinoma of the pyloric end of the stomach was found. Since the only evidence of extension was into the head of the pancreas a subtotal gastric resection (three-quarters of the stomach) was performed, together with removal of the head of the pancreas and duodenum. A retrocolic pancreaticojejunostomy and choledochojejunostomy was performed, and an antecolic long loop gastrojejunostomy. Drainage to the right gutter was established through a stab wound.

Postoperative Course: Unremarkable. The patient was discharged well on the 14th postoperative day. At two months he is entirely well, having gained over 15 pounds.

SUMMARY

(1) Five previously unreported cases of carcinoma involving the head of the pancreas which have been treated radically are recorded.

(2) Some form of pancreaticojejunostomy following partial pancreatic-

otomy is recommended, and a method is outlined which has proved satisfactory in four cases.

(3) A case of subtotal gastric resection and radical pancreaticoduodenectomy for carcinoma of the stomach invading the head of the pancreas is reported.

(4) Various other problems associated with radical extirpation of cancer involving the head of the pancreas are discussed.

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NEUROGENIC SARCOMA OF THE JEJUNUM ASSOCIATED WITH VON RECKLINGHAUSEN'S DISEASE

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REPORTED INSTANCES of neurogenic sarcoma of the small intestine are rare. The following account deals with such a lesion in the jejunum, discovered by preoperative roentgenograms and successfully resected. The patient also had von Recklinghausen's disease, with multiple cutaneous and subcutaneous nodules and scoliosis of the dorsolumbar spine. The jejunal tumor did not cause obstruction but first gave notice of its existence through small hemorrhages.

Case Report.—A 37-year-old, white, male officer was transferred to an Army General Hospital because of intestinal hemorrhage and secondary anemia. About six weeks previously he had first noticed the passage of dark blood in his stools. At that time he also was having cramp-like abdominal pains in the lower left quadrant, relieved by heat, but no constipation or diarrhea. On admission to a Station Hospital, April 30, 1943, the R. B. C. was 2.5 million; W. B. C. 4,800; urinalysis and Kahn test negative, and stool positive for occult blood. No tenderness or masses were found on abdominal examination. During his stay there, a G.-I. series and two barium enemas, including air-contrast study of the colon, were all reported negative. One week after admission the R. B. C. was 3.3 million, with 46 per cent hemoglobin. This secondary anemia responded to therapy with iron and liver extract. Occult blood continued to be present in the stools.

On May 29, the patient had a sudden large intestinal hemorrhage, and was found lying in a pool of fresh blood and clots which he had passed by rectum. The R. B. C. dropped from 3.3 to 2.7 million, and the hemoglobin from 60 to 55 per cent. The next day sigmoidoscopy was done but no abnormalities were found.

One week after the hemorrhage, June 5, 1943, he was transferred to a General Hospital. The stools were positive for occult blood for the next ten days but negative thereafter. Aided by iron therapy his anemia steadily improved. Roentgenologic studies of the upper gastro-intestinal tract revealed a large filling defect, approximately in the upper half of the jejunum, with moderate dilatation of the intestine above it (Fig. 1). This seemed to be caused by a tumor projecting both into the lumen and outwards beneath the serosa. It was causing relatively little obstruction and the barium readily passed by, outlining the fungating intraluminal portion. A roentgenogram of the chest showed the lung fields to be clear.

This jejunal tumor was considered to be a neurofibroma or neurogenic sarcoma, a part of the generalized von Recklinghausen's disease with which the patient was afflicted (Fig. 2). There were innumerable small and medium-sized nodules in and beneath his skin, mostly on the chest and abdomen. Some were solid, others felt cystic, still others were pendulous tabs; among them were numerous patches of brown pigmentation. He first noticed the nodules about six years ago, and they continued to appear over a period of two years. The history records no other instance of von Recklinghausen's disease in his family.

FIG. 1.—Roentgenogram from a small intestine series, showing the large filling defect in the jejunum caused by the neurosarcoma. Note the moderate dilatation of the intestine above the lesion. The arrows point to the outer edge of the tumor, which projected into the peritoneal cavity.

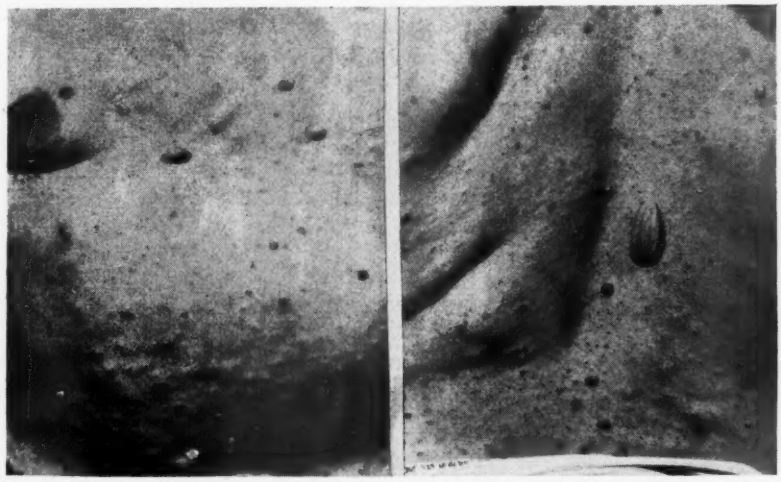


FIG. 2.—Photographs of the anterior and posterior aspects of the chest, showing the typical cutaneous lesions of von Recklinghausen's disease.

The patient also had rather marked scoliosis of his dorsolumbar spine, which had been present since childhood but had never caused him pain or restricted his activities. Roentgenograms during his hospital stay showed the curvature but no congenital anomaly, and no evidence of an inflammatory or destructive process. A survey of the other bones and joints revealed no significant abnormal changes.

Two of the superficial lesions were removed for microscopic study. One of them was a hard, movable, subcutaneous nodule composed of firm, yellowish-gray tissue. Microscopically, there was "rather loose fibrous tissue surrounded by a dense hyalin fibrous tissue capsule." Many of the cells were spindle-shaped, and this arrangement resembled that seen in a neurofibroma. The other was a cutaneous pedunculated growth, "composed of loose edematous fibrous tissue covered with ordinary epithelium."

An abdominal operation was later performed and the jejunal tumor resected. On opening the peritoneal cavity, no free fluid was encountered, and the liver, spleen, kidneys, stomach, and large bowel were normal. In the upper jejunum, approximately two feet below the ligament of Treitz, there was a tumor involving the antimesenteric border of the bowel, about three inches in diameter, with enlarged soft lymph nodes distributed throughout the adjacent mesentery and in the aortic group. One piece of omentum was adherent to the bowel and was freed. The tumor and two inches of bowel on each side were excised and a side-to-side anastomosis constructed.

Pathologic Examination.—Gross: The specimen was opened along the mesenteric border, disclosing a large, fungating tumor mass, 7.5 x 6.5 x 3 cm. in size, projecting into the lumen (Figs. 3 and 4). The mass was canalized so that there was a ring of tumor tissue around the entire circumference within the bowel, though attached to the wall only at its base (Fig. 5). Two channels were thus present, a small one through the tumor, about 1.5 cm. in diameter, and a narrow slit between the free edge of the tumor and the uninvolved intestinal wall. No frank ulceration was noted. The tumor also projected from the serosa, forming an irregular, lobulated mass about 5 cm. in diameter. No lymph nodes were included with the specimen.

Microscopically (Fig. 6), the tumor was "composed of cells having elongated spindle-shaped or fusiform nuclei arranged in interlacing strands or bundles. The tumor is quite cellular. There is very little anaplasia. A few irregular mitoses are present. Although the tumor appears relatively benign, the cellularity and mitoses indicate that it should probably be considered as a neurogenic sarcoma. *Pathologic Diagnosis:* Neurogenic sarcoma of jejunum."

This histologic diagnosis was confirmed by the Army Medical Museum, with the additional observation that "from the clinical standpoint there should be no further complication from the removal of this tumor since such tumors rarely metastasize."

The patient rapidly recovered from the operation, and there were no complications during the postoperative period. Within three weeks the wound was entirely healed and the patient was ambulatory, eating his meals and gaining weight. After a month's sick leave, he was in excellent condition and returned to his duties.

We have not attempted to make a complete list of reported gastrointestinal neurogenic sarcomas but believe a partial account would be interesting. According to Ewing,[1] Sarazanes collected reports of such tumors affecting the tongue, stomach, jejunum, ileum, and colon.

Hosoi's[2] study of the literature revealed five cases which are considered neurosarcoma, though originally some were given other names:

Adrian (1902). Fibrosarcoma of the duodenum, associated with multiple fibromas of skin and internal viscera and neuromyxoma of supraclavicular fossa.

Kohtz (1893). Sarcomatous tumor of duodenum, nodules on surface of stomach and several subserous nodules in small intestine and mesentery.

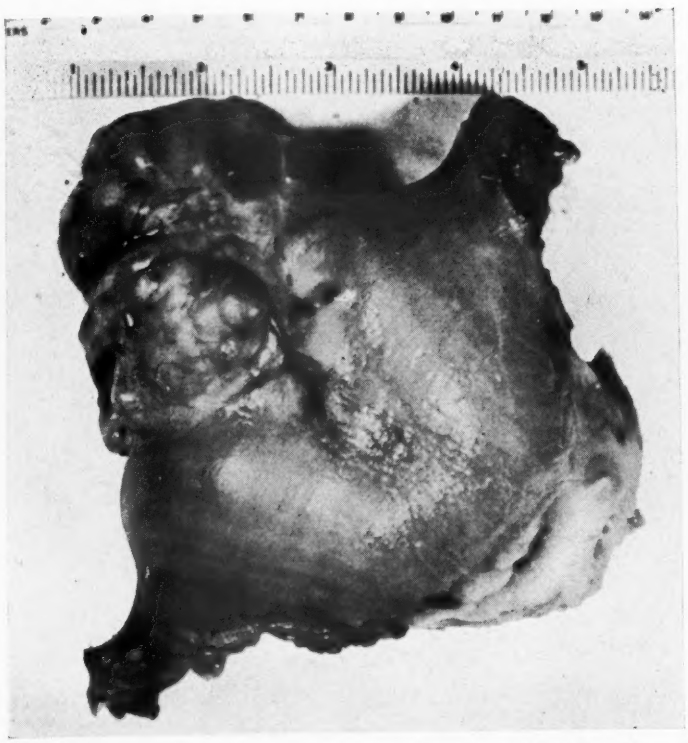


FIG. 3.—Photograph of the excised tumor, showing the lobulated, subserosal portion which protruded into the peritoneal cavity.

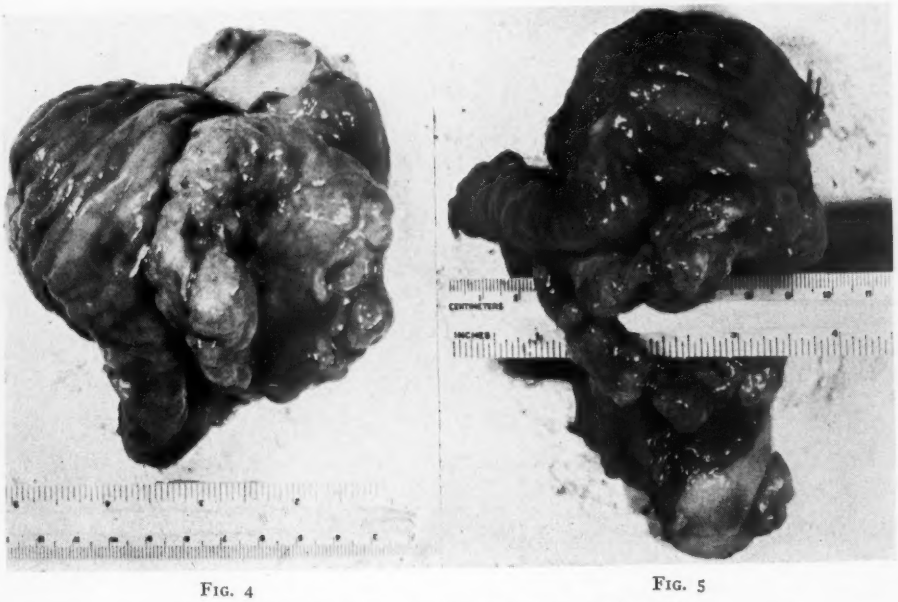


FIG. 4

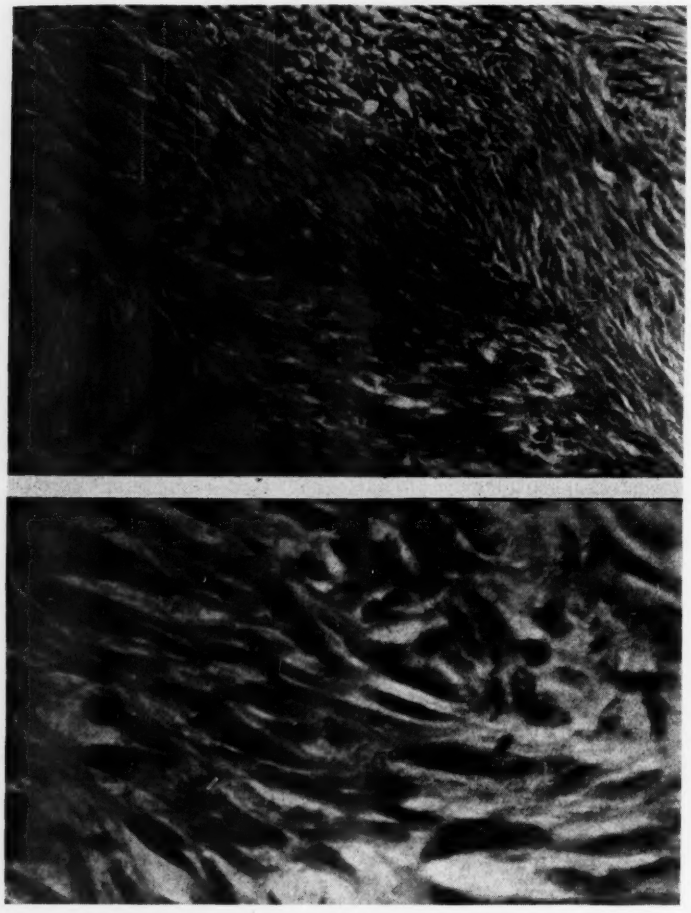
FIG. 5

FIG. 4.—The fungating, intraluminal portion of the sarcoma.
FIG. 5.—A ruler has been passed through the extra lumen formed by canalization of the tumor.

Shouldice (1925). Fibromyxosarcoma on greater curvature of stomach, in a case with multiple peripheral fibromas and many millet-seed, nodular tumors on surface of stomach.

Hartman (1927). Fibromyxosarcoma of stomach, believed to have arisen in a neurofibroma of the gastric wall, in a patient with von Recklinghausen's disease.

(a)



(b)

FIG. 6.—(a) Photomicrograph of the jejunal neurosarcoma, showing the nuclei arranged in interlacing strands and bundles.
(b) High power view, showing the spindle-shaped and fusiform nuclei. The tumor is quite cellular, though there is very little anaplasia.

von Recklinghausen (1882). Sarcoma of jejunum in a case of neurofibromatosis (two of the largest nodules on the jejunum were sarcomatous).

Geschickter,[3] in his analysis of 1472 malignant tumors of the gastrointestinal tract, found 50 cases of sarcoma, ten of which were "nerve sheath sarcomas." Of these ten, three were in the stomach, three in the small intestine and four in the rectum; one of the small intestinal sarcomas was associated with von Recklinghausen's disease. Bergendall and Sjövall[4] reported

a case of resected neurinoma of the ileum, 8 cm. in diameter, which had ruptured from central necrosis and given rise to acute peritonitis. Three years after removal of the tumor, generalized abdominal metastases developed. At autopsy, the disseminated peritoneal lesions were said to show the characteristic histologic aspects of neurinoma, but malignant alteration was indicated by the numerous mitotic figures.

Miller and Frank[5] present two well illustrated case reports of "neurofibrosarcomas" of the jejunum. In the first (a female, age 72, with no personal or family history of von Recklinghausen's disease), there was a large, lobulated, medullary tumor attached to the antimesenteric border of the jejunum. Six months after resection she was reported well. The second case (a male, age 47, also without family history of von Recklinghausen's disease, and without cutaneous lesions), presented a large mass beneath the ligament of Treitz and multiple tumors of the jejunum and ileum, mesentery, and retroperitoneal nodes. Most of them (about 26) were in the intestinal wall, varying in diameter from 0.5 cm. to 10 cm., projecting either inward or outward. A few were ulcerated and one large lesion, at autopsy, formed a "truncated tumor, replacing the bowel, with a lumen through it." The microscopic diagnosis was neurofibrosarcoma, multiple, of small intestine, with metastases to mesenteric and retroperitoneal lymph nodes.

Grill and Kuzma[6] have recently reported an interesting case, though not of a sarcoma. Theirs was a large ileal neurofibroma in a patient with von Recklinghausen's disease. The tumor was the origin of severe, intermittent, intestinal hemorrhages, which finally caused death. It arose in the wall of the ileum and protruded into the peritoneal cavity, drawing a pouch of epithelium with it. Many thin-walled blood spaces next to the intestinal epithelium, some of them eroded, were apparently responsible for the bleeding. The authors included an extensive bibliography, together with a discussion of benign intestinal tumors and von Recklinghausen's disease.

Discussion.—The whole subject of neurofibromatosis, tumors of peripheral nerves and neurogenic sarcoma is complex and controversial. The main features of von Recklinghausen's disease are well known, but the associated skeletal, visceral and endocrine manifestations are ill defined. Problems of histogenesis are unsettled and classifications are numerous, elaborate and conflicting. Some authors hold that the Schwann cell plays the predominant part in the growth of neurogenic sarcoma while others believe it is the fibroblast. For a lucid, authoritative review, in which the various threads of discussion and debate are skillfully drawn together, we recommend the chapter in the treatise by Ewing.[1]

In von Recklinghausen's disease several types of lesions are encountered. The most common and characteristic are the multiple cutaneous and subcutaneous neurofibromas; similar multiple tumors are also found along the deeper nerves and in the mucous and serous membranes and viscera. In the skin the nodules are usually accompanied and often preceded by coffee-colored areas of pigmentation. Two other types of lesions are the plexiform neuroma

and elephantiasis neuromatosa. Occasionally, there is also the neurinoma, though this is more often solitary. This is an encapsulated tumor, mainly of the larger nerve trunks, occurring in the subcutaneous and muscular tissues of the limbs and in various internal structures. It has a distinctive histologic pattern ("palisade units"). Neurogenic sarcoma, or neurosarcoma, develops in about 13 per cent of the cases of von Recklinghausen's disease, according to Hosoi.[2] In addition, many other organs and systems are directly or indirectly affected as a part of the disease—brain, meninges, spinal cord, vascular system, cutaneous structures, and bones. The osseous changes[7, 8] are frequent and include scoliosis (most common), localized hypertrophy and other abnormalities of growth, and subperiosteal cysts.

Our patient had the typical cutaneous and subcutaneous neurofibromas, mostly on his trunk. Among them were numerous pigmented areas of *"café au lait"* color and probably some small lipomas and fibromas. There was no plexiform neuroma or elephantiasis. He had a marked scoliosis but no other bony abnormalities. Although many cases of von Recklinghausen's disease are inherited, there is no recorded history of the malady in our patient's family.

The most interesting feature of the case is the neurosarcoma of the jejunum, especially its location. Malignant tumors of the nerve trunks are not uncommon and they may occur anywhere. The great majority, however, show a predilection for the subcutaneous and deeper intermuscular tissues of the limbs, including the shoulders and hips. Only a few neurosarcomas have been described in the gastro-intestinal tract, and jejunal examples are quite rare.

In this location they arise in the wall of the intestine, protruding into the lumen or outward into the peritoneal cavity. Often they grow in both directions, as in our case. The mucosa covering the intraluminal growth may be intact or ulcerated. When ulceration is present, the resultant hemorrhage may be very severe. Intestinal obstruction has occurred, but it has usually been incomplete, since these sarcomas are fungating rather than annular and constricting. In our case, an additional safety factor was a narrow channel running through the polypoid tumor, providing a second and extra lumen for the passage of the intestinal contents. The tumors may cause intussusception, as illustrated by Miller and Frank's[5] second case. They may also perforate, especially if the interior of the sarcoma is necrotic (Bergendal and Sjövall[4]).

Neurogenic sarcomas frequently occur in conjunction with von Recklinghausen's disease. In Stewart and Copeland's[9] series of neurosarcomas, 21 out of 104 cases (20 per cent) were associated with one or more stigmata of the generalized disease. Stout[10] maintains the incidence is very much higher, and that careful search and recording will establish the presence of pigmentation or a few skin tumors in many more cases. The majority of these malignant tumors, he believes, develop in preexisting neurofibromatous nodules, though this is often difficult or impossible to prove. The neurinomas rarely become malignant.

The anatomic, microscopic and clinical features of neurogenic sarcomas are fully described by the above authors[9, 10] and Geschickter,[11] and summarized by Ewing. Most of this knowledge has accumulated from study of sarcomas of the peripheral nerve trunks, which are by far the most numerous. Briefly, the features are: (1) Sudden, rapid enlargement of an old tumor; (2) prolonged, persistent growth; (3) recurrence in original site after incomplete removal; (4) frequent appearance, after local excision, of a new tumor or tumors higher up the same nerve trunk, either arising independently, or from extention along the nerve within the epineurium; (5) complications and death may occur from the local lesion, because of ulceration, infection, hemorrhage, or invasion of vital structures; (6) metastasis in about 20 per cent of cases, usually hematogenous to lungs; (7) rare involvement of regional lymph nodes; (8) better prognosis of encapsulated tumors; and (9) wisdom of amputation after repeated occurrences. Ewing divides the tumors into three histologic types: Sclerosing, spindle cell, and cellular anaplastic neurosarcomas. The tumor in our case fits into the second, intermediate, type.

The treatment and prognosis are also discussed by these authors. Ewing[1] concludes with the statement: "On account of the bad prognosis of most sarcomas of the soft parts, and the radiosensitivity of many, especially the more malignant ones, a program should be adopted of diagnosis by aspiration and thorough radiation before surgery is employed."

SUMMARY

A case is presented of neurogenic sarcoma of the jejunum in a patient with von Recklinghausen's disease. The tumor caused intestinal bleeding, and was successfully resected.

The rarity of this type of tumor in the jejunum, its association with von Recklinghausen's disease, and the general subject of neurogenic sarcomas are briefly discussed.

The authors extend their thanks to Lt. Col. John M. Wellman, M.C., the surgeon who performed the operation, and to Lt. Col. Perry T. Hough, M.C., the pathologist, for their cooperation in assembling data for the case report.

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ESTIMATION AND SIGNIFICANCE OF BLOOD LOSS DURING GASTRO-INTESTINAL SURGERY*

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Although by the application of newer surgical technics the problem of blood loss during operations has ceased to be formidable, nevertheless its accurate estimation is frequently worth while. This is particularly true in anemic patients with cardiovascular insufficiency. These individuals sometimes cannot spare even a small amount of blood, yet its replacement by transfusions, when overestimated in amount, may induce cardiovascular collapse.

The determination of blood loss cannot accurately be made from the postoperative concentration of hemoglobin or the red cell count. It is a well-proven fact that the total blood volume is very labile, and after operative hemorrhage it frequently may shrink in an attempt to maintain the preoperative concentration of blood. A comparison of the pre- and postoperative blood counts, therefore, cannot be substituted safely for an accurate estimation of the blood shed during surgical procedures. Since the repeated determination of total blood volume *in vivo* is often a difficult procedure, the more feasible determination is the direct measurement of blood loss.

Quantitative determinations of blood loss during some common operative procedures were made by Gatch and Little.[1] The method employed by these investigators was to wash promptly and repeatedly all sponges and instruments soiled with blood. Enough hydrochloric acid was then added to the pooled washings to make a final 0.1 N solution. The resulting acid hematin was compared with a standard solution of acid hematin prepared from the whole blood of the patient before operation.

More recently, White and Buxton[2] employed a modification of the acid hematin technic to determine blood loss during intrathoracic surgical procedures. Their method entailed the recovery of all blood from linens, sponges, and instruments by extraction with distilled water. Nine cubic centimeters of this solution were converted to acid hematin by the addition of 1 cc. of 1 N hydrochloric acid. This last solution then was compared colorimetrically with a standard prepared from 1 cc. of the patient's blood in which the hemoglobin was converted to acid hematin by the addition of 9 cc. of 0.1 N hydrochloric acid. By this technic about 86 per cent of the hemoglobin could be recovered.

* Read before the New York Surgical Society, December 8, 1943. Paper No. 22 in a series of metabolic studies on patients with cancer of the gastro-intestinal tract.

A simple and ingenious approach to the problem recently was offered by Wangensteen.[3] The gain in weight of a known amount of dry linens and sponges used during operation is converted into cubic centimeters of blood absorbed by reference to the specific gravity of the patient's blood. The technic is claimed to be accurate to within a few per cent. Moreover, the use of dry sponges apparently does not impose a serious handicap to the surgeon. Large packs which are kept moist to keep a minimum of fibrin formation on the bowel are employed to cover the intestine. The method offers the further advantage that at any time during the operation the surgeon can be informed of the blood lost up to that point. By this procedure, Wangensteen has found that the usual blood loss consequent to gastric resection varies from 300 to 500 cc.

In the present study an attempt has been made to incorporate the best features of the above methods, and at the same time to keep the technic simple enough to be employed by the average hospital technician.*

METHOD

All blood-soaked linen and sponges are meticulously collected in a single container. As soon after the end of the operation as possible, the blood is extracted from these materials by the repeated addition (ten times) of tap water. All washings are pooled, and the total volume measured. An aliquot of this is filtered and provides the solution for measurement in a photoelectric colorimeter (Klett-Summerson, Filter No. 52).

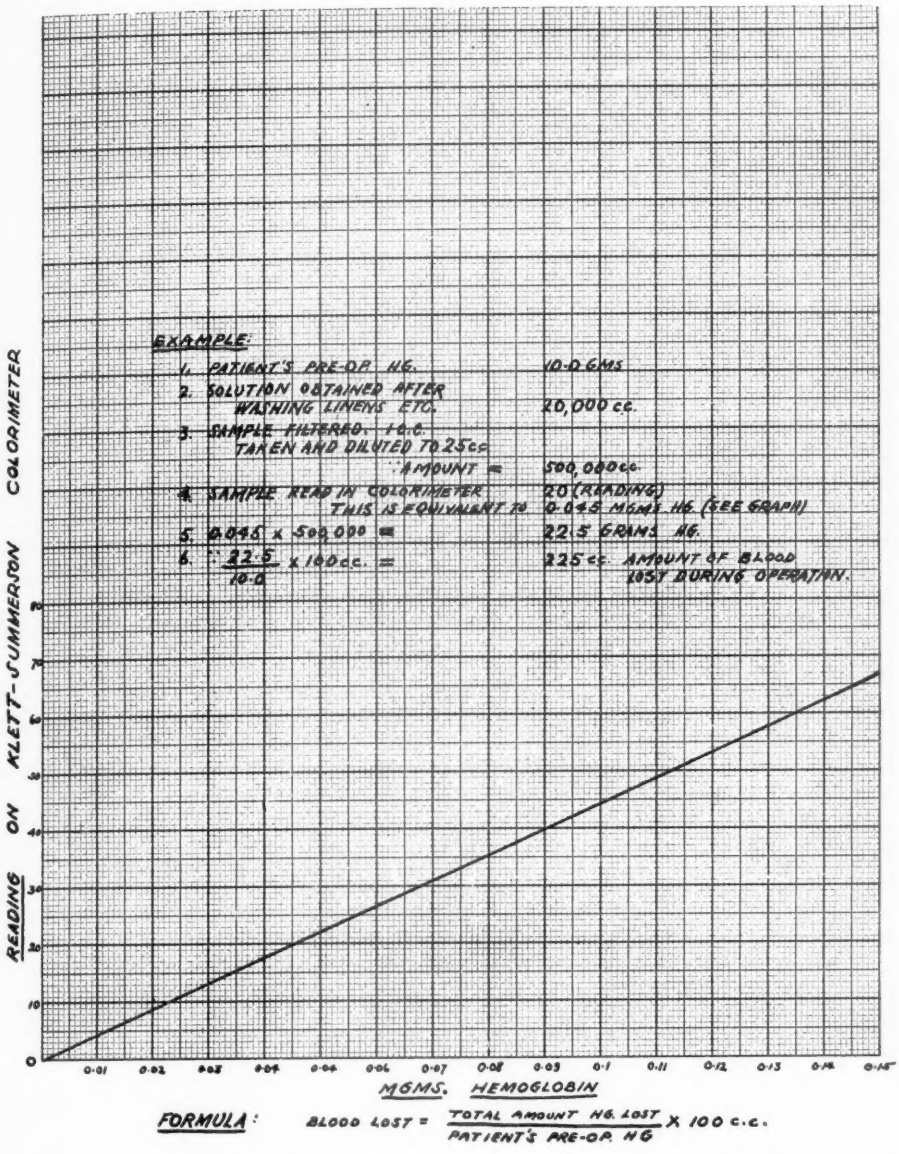
The standard curve for this comparison is constructed by the measurement of several dilutions of a normal blood found to contain 13.8 Gm. of hemoglobin by the Sahli technic.[4]

The concentration of hemoglobin in the blood of the patient is necessarily determined preoperatively. From these values, it is possible to ascertain the volume of blood lost during the surgical procedure. A sample calculation is appended:

Sample:	1. Patient's preoperative hemoglobin.	10 Gm. per cent
	2. Volume of solution obtained after washing linens, *etc.*	20,000 cc.
	3. Sample filtered. It was deemed necessary to dilute one cc. of this to 25 cc. since the reading lay outside the graph limits. Therefore, the total amount of hemoglobin solution is (This is not always a necessary step.)	500,000 cc.
	4. Sample is read in the Klett-Summerson colorimeter. The reading is	20
	From standard curve, this represents	0.045 mg. Hb.
	5. 0.045 x 500,000 equals	22.5 Gm. Hb.
	6. Therefore: $\frac{22.5}{10}$ x 100 cc. equals the amount of blood lost during the operation	225 cc.

*All operations listed were performed by a single surgeon (G. T. P.) so the comparative values of blood loss should be significant.

CHART I



FORMULA: BLOOD LOST = $\frac{\text{TOTAL AMOUNT HG. LOST}}{\text{PATIENT'S PRE-OP. HG}} \times 100$ c.c.

The accuracy of the method was determined by the recovery of known quantities of blood from samples of linen and sponges. The hemoglobin recovered aften ten washings was found to vary from the known amount by no more than 6 per cent.

RESULTS

A. BLOOD LOSS DURING OPERATIONS TO SERVE AS CONTROL DATA FOR GASTRO-INTESTINAL PROCEDURES:

Information concerning the quantity of blood lost during operation chiefly for cancer of the gastro-intestinal tract becomes more valuable and significant

when the figures so obtained are compared with the blood loss sustained during other common operations performed by the same surgical team. From this viewpoint of blood loss, the average major operation on the gastro-intestinal tract compares favorably with such procedures as hip joint disarticulation (300 cc.) and splenectomy (160 cc.). Hysterectomy, on the other hand, is a relatively bloodless operation. Radical vulvectomy with bilateral groin dissection (725 cc.) and radical mastectomy (average 600 cc.) entail a considerable blood loss with minor shock in spite of scrupulous care to maintain hemostasis (Table I).

TABLE I

CONTROLS

Patient	The Following Operations Used to Standardize Procedure: Operation	Hb. 13.8 Gm. = 100 Per Cent	Blood Loss Cc.	Surg. Est. Cc.	Trans. Cc.	Hb. First Day Postop.
F. S.	Bilateral groin dissection and vulvectomy	9.7	725	600	640	9.8
T. B.	Hip disarticulation	11.0	300	150	600	....
J. G.	Amputation midthigh without tourniquet	11.0	410	350	0	....
G. O.	Radical mastectomy	11.0	650	1200	0	9.7
D. M.	Radical mastectomy	9.7	475	500	600	8.3
B. T.	Radical mastectomy	11.7	700	500	250	10.2
M. B.	Splenectomy	9.5	160	150	600	13.0
G. B.	Supracervical hysterectomy and appendicectomy	10.2	40	50	0	....
C. B.	Supracervical hysterectomy, appendicectomy and bilateral salpingo-oophorectomy	10.2	90	100	0	10.2
B. M.	Supracervical hysterectomy	13.5	135	175	0	....
M. H.	Panhysterectomy	9.7	165	175	0	....
A. B.	Resection jejunal diverticulum	11.0	50	100	695	9.0

B. GASTRO-INTESTINAL OPERATIONS

The amount of blood lost during the simple procedure of gastrostomy or enterostomy varied only from 15 to 75 cc. (Table II). In one instance, however, the formation of a Spivack gastrostomy entailed a loss of 305 cc.; inasmuch as this procedure was employed for a markedly adherent and inoperable cancer of the gastric cardia, this value was not unexpected.

TABLE II

THE BLOOD LOSS DURING PALLIATIVE OPERATIONS FOR GASTRIC CANCER

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
R. H.	Janeway gastrostomy for ca. cardia	11.0	75	150	None	....
H. P.	Spivack gastrostomy for ca. cardia	11.7	305	300	600	11.7
F. P.	Beck-Jianu gastrostomy for ca. cardia	9.7	50	50	600	9.7
J. B.	Jejunostomy for ca. stomach	13.8	15	25	600	10.4
A. H.	Gastro-enterostomy	11.7	45	75	None	10.2
J. F.	Exclusion operation and gastrojejunostomy for ca. stomach	9.3	100	150	600	10.2
J. O.	Exclusion operation and gastrojejunostomy for ca. stomach	13.0	250	300	600	12.0
	Average		120			

The average amount of blood lost during total gastrectomy was only 194 cc. (Table V). This is even less than that found for the group submitted to subtotal gastrectomy for cancer, namely 234 cc. (Table IV). The explan-

ation of this difference can be attributed to the small amount of bleeding encountered during transsection of the abdominal esophagus as compared with the much wider transsected stomach. The transthoracic approach for operable cancers of the cardia apparently does lead to a considerable blood loss, namely 450 and 475 cc. in two instances in which this was determined

TABLE III

THE BLOOD LOSS DURING SUBTOTAL GASTRIC RESECTION FOR ULCER

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
M. Mc.	Subtotal gastric resection for ulcer	11.7	270	200	650	12.1
F. S.	Subtotal gastric resection for ulcer	11.3	305	600	600	13.4
W. O.	Subtotal gastric resection for ulcer	12.1	250	300	600	13:9
W. G.	Subtotal gastric resection for ulcer	10.2	160	300	600	10.9
S. S.	Subtotal gastric resection for ulcer	11.5	150	200	None	10.5
M. A.	Subtotal gastric resection for ulcer	9.3	500	700	600	8.3
B. R.	Subtotal gastric resection for ulcer	7.6	250	350	600	11.0
R. R.	Subtotal gastric resection for ulcer	11.0	320	250	600	12.4
R. G.	Subtotal gastric resection for ulcer	10.1	300	375	600	11.7
G. A.	Subtotal gastric resection for ulcer	11.3	160	175	600	....
	Average		267			

TABLE IV

THE BLOOD LOSS DURING SUBTOTAL RESECTION FOR GASTRIC CANCER

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
A. V.	Subtotal resection for ca.	13.1	300	700	600	12.1
A. F.	Subtotal resection for ca.	13.1	365	275	600	12.4
F. M.	Subtotal resection for ca.	13.5	175	200	600	9.2
E. M.	Subtotal resection for ca.	10.4	160	160	600	10.9
E. D.	Subtotal resection for ca.	11.7	190	250	600	11.7
B. M.	Subtotal resection for ca.	7.3	225	175	650	8.1
M. L.	Subtotal resection for ca.	8.1	250	175	650	10.8
S. L.	Subtotal resection for ca.	9.7	210	200	600	10.9
	Average		234			

(Table VI). The greater part of this blood loss occurs in making the necessarily long intercostal incision.

The average amount of blood lost during subtotal gastrectomy for ulcer (Table III) was not significantly different from that for subtotal gastrectomy for gastric cancer. It might have been expected that the control of bleeding in patients with gastro-intestinal cancer would have been a more difficult problem since these individuals have a high incidence of hypoprothrombinemia.[5]

The procedures of hemicolectomy and sigmoidectomy do not entail a great loss of blood. The average values found were 143 and 124 cc., respectively (Tables VII, VIII). Abdomino-perineal rectal resections have proven almost consistently to be relatively bloody operations (Table IX). It is not unusual for the patient to lose about 400 cc. during this procedure.

COMMENT.—The accompanying tables indicate the almost constant practice of administering a blood transfusion during the course of operations for cancers of the gastro-intestinal tract. In practically every instance, however, the usual transfusion of from 500 to 600 cc. restores more blood to the patient

than is lost during the operation. The blood given at this time is invaluable and probably is of greater value than blood given during the period of preoperative preparation. This observation is based, of course, on clinical experience, and it is common practice today for surgeons doing this type of work seldom to request a preliminary blood transfusion unless the patient's hemo-

TABLE V

THE BLOOD LOSS DURING TOTAL GASTRECTOMY FOR GASTRIC CANCER

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
M. L.	Total gastrectomy for ca.	11.5	175	300	650	10.9
H. M.	Total gastrectomy for ca.	7.6	150	200	600	8.1
D. E.	Total gastrectomy for ca.	8.4	180	250	900	8.6
E. A.	Total gastrectomy for ca.	11.5	270	225	650	10.4
	Average		194			

TABLE VI

THE BLOOD LOSS DURING TRANSTHORACIC RESECTION FOR CANCER OF GASTRIC CARDIA

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
L. H.	Transthoracic resection for ca. cardia	12.0	450	450	1200	12.0
C. K.	Transthoracic resection for ca. cardia	11:0	475	450	1200	8.6
	Average		463			

TABLE VII

THE BLOOD LOSS DURING RIGHT HEMICOLECTOMY FOR CANCER

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
A. W.	Hemicolectomy for ca., with ileotransversostomy (anastomosis)	9.3	30	125	600	10.6
B. K.	Hemicolectomy for ca., with ileotransversostomy (anastomosis)	9.9	160	300	650	10.8
A. K.	Hemicolectomy for ca., with ileotransversostomy (anastomosis)	11.0	230	350	600	10.8
A. K.	Hemicolectomy for ca., with ileotransversostomy (anastomosis)	10.4	170	250	600	10.4
G. S.	Hemicolectomy and external ileocolostomy	9.0	125	300	600	7.5
	Average		143			
R. G.	Cecostomy	10.8	30	30	600	9.7

globin is below 60 per cent. Previous studies from this service[5] have indicated that the best way to combat the anemia is to remove the cancer, after which the restoration of the blood picture to normal occurs spontaneously.

In each of the tables presented, a column is included to indicate the surgeon's estimate of the blood lost during each operation. During the early phase of the study, this estimate often was grossly inaccurate. It is altogether likely that other surgeons in other institutions without means to measure accurately the actual blood loss, would be equally wrong in their clinical evaluation of the bloody or bloodless character of a given procedure. However, accurate judgment is speedily acquired both during and after the operation, and this ability, once gained, can be a valuable part of the surgeon's training.

TABLE VIII

THE BLOOD LOSS DURING SIGMOIDECTOMY FOR CANCER

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
S. L.	Resection of rectosigmoid and permanent colostomy	10.4	340	250	600	10.7
C. H.	Sigmoidectomy and Mikulicz colostomy	12.1	75	100	600	11.7
S. R.	Sigmoidectomy and Mikulicz colostomy	11.6	100	150	600	10.8
M. K.	Sigmoidectomy and Mikulicz colostomy	9.6	75	125	600	11.0
I. P.	Sigmoidectomy and Mikulicz colostomy	11.0	75	150	600	10.7
M. P.	Sigmoidectomy with end-to-end anastomosis	13.7	75	75	600	10.0
P. P.	Sigmoidectomy with end-to-end anastomosis	11.0	125	225	600	10.8
	Average		124			
A. B.	Colostomy	11.0	23	15	600	10.2
S. S.	Colostomy	6.6	10	15	600	9.3

TABLE IX

THE BLOOD LOSS DURING ABDOMINO-PERINEAL RECTAL RESECTION FOR CANCER

Patient	Operation	Hb. Gm. Per Cent Preop.	Blood Loss Cc.	Surg. Est. Cc.	Blood Given at Operation	Hb. Gm. Per Cent First Day Postop.
A. S.	Without colostomy and with preservation of sphincter	11.7	400	300	650	11.0
L. R.	Without colostomy and with preservation of sphincter	12.4	400	500	800	11.7
J. L.	Abdomino-perineal resection	11.5	535	700	600	9.9
P. R.	Abdomino-perineal resection	11.0	735	1200	690	9.2
H. H.	Abdomino-perineal resection	11.0	325	400	650	10.8
A. M.	Abdomino-perineal resection	8.1	250	275	600	9.2
H. M.	Abdomino-perineal resection	12.8	250	500	600	9.9
S. S.	Abdomino-perineal resection	11.6	450	375	600	10.4
H. S.	Abdomino-perineal resection	11.7	350	450	600	12.3
	Average		411			
M. S.	Panhysterectomy, partial vaginectomy and abdomino-perineal rectal resection, with preservation of sphincter	6.9	900	1000	600	8.3

The values to the surgeon of having the blood loss measured for the operations he commonly performs are several: (1) He achieves an accuracy in his clinical estimation of the amount of blood lost during any operation. (2) This knowledge breeds a constant consciousness of the degree of blood loss so that he is not painfully surprised at unexpected shock or collapse. Proper measures, therefore, are introduced in time to prevent such complications. (3) The young surgical intern or resident is furnished with figures which he may use to compare with the blood loss sustained during his own procedure. In no other way can he be so strongly impressed with his own skill or deficiency in the maintenance of hemostasis.

CONCLUSIONS

1. The amount of blood lost in gastro-intestinal surgery is not excessive and is less than the average in a radical mastectomy. The surgeon's initial estimate of the blood lost during an operation is not always accurate, but improves with experience gained in subsequent operations.

2. The difference between the pre- and postoperative concentrations of hemoglobin cannot be used as an index of blood loss.

3. It is important to ascertain the amount of blood shed during operation

in order not to give unnecessarily great amounts of fluid. This is especially true for elderly patients with cardiovascular insufficiency.

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ENTEROGENOUS CYSTS AT THE ILEOCECAL JUNCTION

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ENTEROGENOUS CYSTS have been described in many portions of the alimentary tract, and various theories have been developed to account for their origin in various localities. However, in this discussion we are concerned only with enterogenous cysts situated at the ileocecal junction. These cysts have been variously described as of diverticular origin and due to remnants of the vitelline duct. They are classified by McLanahan and Stone[1] as submucosal, intramuscular, subserosal, mesenteric and antimesenteric. These authors state that they are most common in the ileocecal region and least common in the rectum. It appears that there exist in the embryo numerous diverticula from which enterogenous cysts may develop. Their widespread distribution militates against the theory of development from an unobliterated omphalomesenteric duct. We may say that cysts arising from the vitelline duct resemble enterogenous cysts but are necessarily limited in distribution. Serial sections of human embryos have disclosed evidence of epithelial sequestration. This may possibly be the source of cyst formation in later life.[2] Drennan[3] observes that cysts and diverticula are in reality different phases of the same process. They result from the growth of a bud or from the prolongation of epithelium which has pushed into the mesenchyme. The solid bud then becomes vacuolated and an opening into the intestine may result. In this case, it is a diverticulum. If no opening occurs, it becomes a cyst. The walls usually contain the elements of intestinal structure. It is unwise to speak of true and false cysts as they vary only in the proportions of different layers.

At this point, one might emphasize the fact that the typical cyst consists of muscularis, submucosa and mucosa. The mucosal epithelium may form a complete lining or may exist in patches and the epithelium may contain glands. It is usually of the columnar variety but may be of the low cuboidal type. The fluid contents are usually pale, or straw-colored, but may be mucoid in character and colorless.

DIAGNOSIS

The diagnosis of enterogenous cysts at the ileocecal junction is manifestly difficult and only by keeping the entity in mind can one possibly arrive at this diagnosis. Roentgenologic studies can be of little help except to show signs of compression, inasmuch as there is no connection with the lumen of the contiguous bowel. Cases have been reported at this location from birth to the age of 30 years, predominantly in females. Hughes and Jones[2] have found that cysts of the last four inches of ileum usually are discovered in the

first year of life but cysts of the cecum are found either in the first six months of life or between the ages of 20 and 30. Given a case of a palpable mass in the right lower quadrant, particularly in a youngster, one must consider the possibility of enterogenous cyst in addition to intussusception, appendiceal abscess, regional ileitis, granuloma of the cecum, and possibly twisted ovarian cyst. In the end, the diagnosis will be made at the operating table.

SYMPTOMATOLOGY

The signs and symptoms may be of three varieties: 1. Those due to local pressure with obstruction to intestinal passage. 2. Pain due to tension within the cyst. 3. Those due to ulceration into a blood vessel with bleeding—this being a rare complication. Any or all of these factors may be present and productive of symptoms.

The presenting symptom is usually pain in the right lower quadrant. The pain may be constant and due only to the tenseness of the cyst or it may be of the intermittent type, due to partial or complete obstruction. There may very well be a constant and intermittent element to the pain. All the signs and symptoms of obstruction may be present, depending on when the patient has been seen. The physical examination will show a tense, globular mass in the right lower quadrant, tender to touch, and usually quite mobile. The mobility of the tumor is usually a striking feature and should make one suspicious of the proper diagnosis. Hughes and Jones, in a series of 34 cases, noted simple obstruction in 14 instances, intussusception in six cases, and volvulus in three cases.

TREATMENT

The most interesting phase of this entity is the treatment. Inasmuch, as the patient usually presents signs and symptoms of an acute abdomen, operative treatment is carried out in most cases as an emergency measure. In most instances the surgeon is confronted with a very sick child, often with some degree of obstruction; and the procedure of choice in such instances is debatable. As a matter of fact, the choice of the proper procedure forms the *"raison d'etre"* of this paper.

The operative treatment resolves itself into four procedures: 1. Intestinal resection, with anastomosis. 2. Enucleation of the cyst. 3. Evacuation of the cyst. 4. Marsupialization of the cyst.

1. *Intestinal Resection, with Anastomosis.*—This procedure is a major procedure to be carried out in a desperately sick child, often in the presence of an intestinal obstruction. We must bear in mind, also, that it is being undertaken for a benign ailment, which, with more conservative treatment, could, at worst, result in a mucous fistula. There is no doubt that the procedure is curative but, perhaps, at a prohibitive price. Hughes and Jones report 14 cases of enterogenous cysts treated by intestinal resection, with 11 deaths and three recoveries. On the other hand, Pachman,[4] in a series of 15 cases treated by

resection, reports 11 recoveries and four deaths, or 26.7 per cent mortality —a remarkable record but still a high mortality rate.

2. *Enucleation.*—This is fraught with danger, inasmuch as the cyst is part and parcel of the intestinal wall and cannot be enucleated without opening into the intestinal wall. Opening into the large bowel in the presence of obstruction may easily result in a fatality. Hughes and Jones report a series of nine cases treated in this manner, with five successes and four failures. Drennan states, categorically, that in no case has enucleation been successful. If the cyst is of the intramural type, with which we are concerned, enucleation is manifestly a dangerous procedure.

3. *Evacuation.*—Simple evacuation, or partial resection of the cyst, can only result in its refilling, with an unsuccessful result. One must keep in mind the possibility of leakage into the peritoneal cavity after such a procedure with resultant chemical and possibly bacterial peritonitis. Hughes and Jones report one fatality from this procedure.

4. *Marsupialization.*—Inasmuch, as one is usually dealing with an acute and often desperate situation in a young child, the conscientious surgeon would choose the procedure that relieves the immediate symptoms, gives some hope of primary cure and, if not, will allow a more radical secondary procedure at a future time under more favorable circumstances. Thus, if the tense cyst is emptied of its contents (which should be sterile) the obstructing factor is immediately relieved. However, one must then fix the cyst wall to the abdominal wall, thus marsupializing it and allowing free drainage to the outside. Recovery is usually uneventful. Hughes and Jones report two cases with two recoveries, treated by this method but no mention is made of permanent recovery or persistence of a fistulous tract. Beekman[8] reports a marsupialized case with secondary fistula which was ultimately closed. Pachman reports a series of two cysts at the ileocecal junction treated by marsupialization, with two recoveries.

The use of escharotics to try to obliterate the mucosal lining of the sac, and thus obviate a secondary procedure, does not seem to have been emphasized in the literature. We feel the most logical and least risky method of handling these cases, where at all possible, is marsupialization and subsequent treatment with escharotics. If the fistula fails to close, intestinal resection can always be carried out. At this time one has the obvious advantage of a good-risk patient.

Case Report.—M. N., female, age six, was admitted to the Montefiore Hospital, May 1, 1941, with a 24-hour history of abdominal pain, intermittent in type, associated with emesis. Interrogation revealed the fact that on several occasions during the year previous to admission there had been several episodes of pain, which spontaneously were relieved. The past medical history was otherwise negative. The family history disclosed nothing of note.

Physical Examination.—This disclosed an acutely ill child in evident pain. The abdomen was somewhat distended; peristalsis was active. Palpation in the right lower quadrant revealed a tense, highly mobile, tender mass about the size of a small orange. Immediate operation was performed.

Operation.—The peritoneal cavity was opened through a right rectus incision, and disclosed a mass, cystic in nature and the size of a small orange, at the ileocecal junction, which was apparently producing a partial obstruction of the small bowel. An attempt was made to obtain a plane of cleavage and enucleate the cyst, but it was found to be intrinsically a part of the bowel wall and this could not be done. The cyst was opened and a large amount of mucoid material escaped. On inserting a finger into the lumen one could appreciate that it was not continuous with the bowel lumen. It was decided to marsupialize the cyst and treat it with escharotic solutions later. The cyst wall was fixed to the peritoneum and fascia, and the layers of the abdominal wall were closed loosely around it. One strip of vaselined gauze was placed in the cavity of the cyst. Cultures from the cyst fluid were sterile.

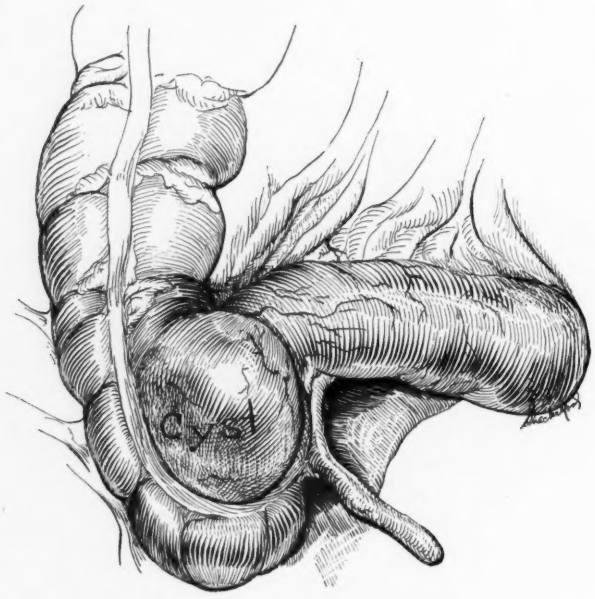

FIG. 1.—Drawing showing the gross appearance of the cyst at the ileocecal junction.

Postoperative Course.—The patient's convalescense was uneventful, and she was discharged 15 days later with a draining mucous fistula.

Subsequent Course.—One month postoperative, treatment with pure carbolic acid and alcohol was instituted; this was continued sporadically, at first weekly and then monthly. At one time sodium morrhuate was tried as the escharotic agent. The amount of drainage gradually lessened but a tract was still present. From time to time the tract would close over but would eventually open again. A lipiodol injection about eight months postoperative, disclosed a small sac, the size of a walnut, still present. Shortly after this (about nine months postoperatively) spontaneous closure resulted.

The child remained in good health until two years later, May 15, 1943, when she complained of pain in the right lower quadrant and a tender mass could be palpated in the scar. Incision and drainage revealed a moderate amount of chocolate-colored material, with no mucoid substance present. The culture was positive for staphylococcus. Drainage persisted for about three weeks and closure resulted. There has been no recurrence at this writing (eight months later). Apparently, the mass was due to a collection of old blood, the source of which would be difficult to determine.

SUMMARY AND CONCLUSIONS

A review of the literature reveals the fact that enterogenous cysts at the ileocecal junction are of infrequent occurrence. Radical surgery in the treatment of this entity carries with it an unnecessarily prohibitive mortality and, in our opinion, should not be carried out unless a complication such as gangrenous bowel is present. Simple marsupialization, with subsequent escharotic treatment, carries with it a fair chance of ultimate cure. Elective resection can always be carried out with much less risk to the patient.

An instance of ileocecal cyst in a female child, age six, has been presented. Treatment consisted of marsupialization plus escharotics. The result seems to have justified this conservative procedure.

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DIFFERENTIAL DIAGNOSIS OF CAUSES OF PAIN IN THE LOWER BACK ACCOMPANIED BY SCIATIC PAIN*†

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THE SYMPTOM OF BACKACHE with referred pain along the course of the sciatic nerve has for many years attracted the attention of orthopedic surgeons and industrial surgeons everywhere. Looking back at the evolution in the diagnosis of this condition over a period of 35 years, one cannot help but remember the old days when the diagnosis of "railroad spine" was made in those cases where an injury occurred at the onset of backache, which was not infrequently followed by sciatic pain. This diagnosis was due to the inability of the medical profession to comprehend the underlying pathologic changes which can happen, and which do happen in the lower back. Little effort had been made, judging from the literature, to assign the symptom of pain to any real lesion.

Goldthwaite[1] then propounded his theory of strain, subluxation, or disease of the sacro-iliac joint. As a result of his work much interest was aroused in the subject, and for a few years the literature was filled with the advocation and defense of this theory. The next great step was made by the contribution of Willis,[2] who reported anomalies in 7 per cent of 748 anatomic specimens. He found marked variation in the normal anatomy of the lower spine, particularly at the lumbosacral junction. Willis called attention forcibly, and conclusively, to these variations in the mechanical structure which could account for many of the symptoms and combinations of symptoms exhibited in the lower back. These anatomic variations might also affect the emerging nerves and the ligaments supporting this portion of the spine. His findings rationalized certain conclusions made previously on a clinical basis regarding the causes of low back pain.

In 1916, I stated before the American Roentgenological Society that low back pain and sciatic pain were to be attributed more to strain of the ligaments of the low back than to any other one cause. I pointed out that all the components comprising this part of the anatomy, namely, the fascia, muscles, joints with cartilage and synovia, tendenous attachments, interlacing ligaments, all surround a bony canal through which the peripheral nerves course; that these structures were subject to the same diseases to which like structures in other parts of the body were vulnerable; that inflammatory reaction in these structures was much more prevalent than in like structures in other parts of the body where there was less cause for strain; and that infection, allergic reaction, gout and other forms of toxemia caused by sys-

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temic conditions could and did produce the same symptoms which in recent years have been ascribed to rupture of an intervertebral disk.

If there is one place in the body where a fine differential diagnosis is necessary it is in the low back. Mechanically, the low back is structurally weak for the work it is required to do. It is the fulcrum on which every motion of the body is pivoted. It lies at the junction of a flexible with an inflexible part, namely, the lumbar spine with the sacrum and the ilia. As previously stated, the tissues which compose the low back are subject to the same ills as similar tissues elsewhere in the body. Moreover, the mechanical strain exerted on these tissues is much greater than elsewhere. In addition, more anatomic variations in structure are found in the lumbosacral junction than in any other location. All these factors contribute to making the low back an area where pain can occur with great suddenness and can be caused by various agents.

In the recent literature, neurosurgeons stand out preeminently as contributors to the subject of low back pain accompanied by so-called sciatica. Their approach has been mainly from the standpoint of root pressure from a ruptured intervertebral disk. To one who has been interested in the subject for more than 30 years, and has examined many hundreds of such cases, this viewpoint seems much too narrow. It is not the intention to contend that low back pain is not, or could not be caused by rupture of a disk, with pressure on the roots, but to point out that the same symptoms can be caused through disarrangement or inflammation of other structures. It seems strange that Schmorl[3] who dissected more than 10,000 cadavers, found only two cases of traumatic rupture of the nucleus pulposus, whereas our surgeons have operated upon hundreds of cases for this condition in the last five years. Schmorl found various degrees of degeneration of the disk and ligaments in more than 15 per cent of all specimens. These degenerative changes around the lumbosacral joint were 7 per cent greater in men than in women, which would tend to indicate that heavy labor has an effect on the structures supporting the lower spine.

It is 30 years since I performed my first bone graft for immobilization of the lower spine. For 12 years I have made sections of the joints of this region in every case operated upon, and in every case pathologic changes were found in the cartilage of the joints, associated with varying degrees of inflammatory reaction in the capsules and ligaments adjacent to or extending from the joints. When one considers that the joints at the lumbosacral junction, for their size, carry approximately ten times the weight per square inch that the knee joints carry, and that the mechanical strain exerted by body weight thrusting downward and forward at the lumbosacral joints puts constant pressure on normally formed joints, it is easy to conceive that in abnormal joints this weight is transferred to the ligaments which, in turn, are required to carry the strain. In either case the strain occurs not on the intervertebral disk in the low lumbar region, but on the ligaments and joints posterior to the spinal canal. In flexion, part of this weight is transferred

to the bodies of the vertebrae and the intervertebral disks, which act as a cushion and compress at the same time that the inferior articular facets of the fifth lumbar vertebra move upward on the superior articulations of the sacrum. The posterior ligaments are stretched as the articulations slide. If there is normal elasticity in the ligaments and the capsules of the joints, and the joints are smooth, this sliding motion can be made without discomfort. However, if the ligaments are degenerated and have lost their elasticity, or if the joint surfaces are rough and surrounded by small exostoses at the attachment of the capsules and tendons, this motion can cause pain either from overstretching of the ligaments which are not able to withstand the strain put upon them, or by actually causing minute tears of this fibrous structure. Moreover, the joints can catch and lock, because the gliding motion is absent due to erosion.

Everyone is familiar with such occurrences in other joints which are degenerated or eroded. From the pathologic changes and symptoms which occur in other joints, especially the knees, which are much more easily examined, we know that swelling, locking and severe, sudden, sharp stabbing pain occurs. We can feel the crepitation and we can demonstrate the locking and immobility. From our pathologic studies, we know that the changes in the low lumbar joints do not vary from the lesions frequently found in the knee, elbow or hip. The swelling occurring as a result of ligamentous and joint injury is familiar to all practitioners of medicine. In the joints of the low back the pathologic changes do not differ from those of joints elsewhere in the body, except that swelling of the ligaments and the joint capsule can, and frequently does, narrow the exit of the nerves as they emerge from the spinal canal and foramen, the posterior wall of which is frequently formed by the anterior margin of the articular facets. The joint capsule of the articular facet lies immediately posterior to the nerve at its exit and forms part of the posterior wall of the foramen (Fig. 1).

In a cross-section of the spine at the lumbosacral level (Fig. 2) the normal lumbosacral joints lie at an angle of 45° to 60° to the anteroposterior plane of the body. There is, however, a great variation in the normal, and it is extremely difficult in many individual cases to judge from the roentgenograms whether these articulations furnish adequate support on one or both sides. What is normal for one person may not be considered normal for another. Roentgenograms should be taken from various angles before a decision is made whether the mechanical support between the vertebrae is adequate. One must take into consideration not only the anteroposterior but the horizontal plane of the joints, because as the patient stands the lumbar curve is increased and a joint which looks almost perpendicular in the sitting position will become almost horizontal in the erect position, depending upon the amount of tilt in the pelvis (lordosis) in standing. The more horizontal the articulation, the more strain is put upon the ligaments which support it and the low spine, in general, in the flexed position. Instead

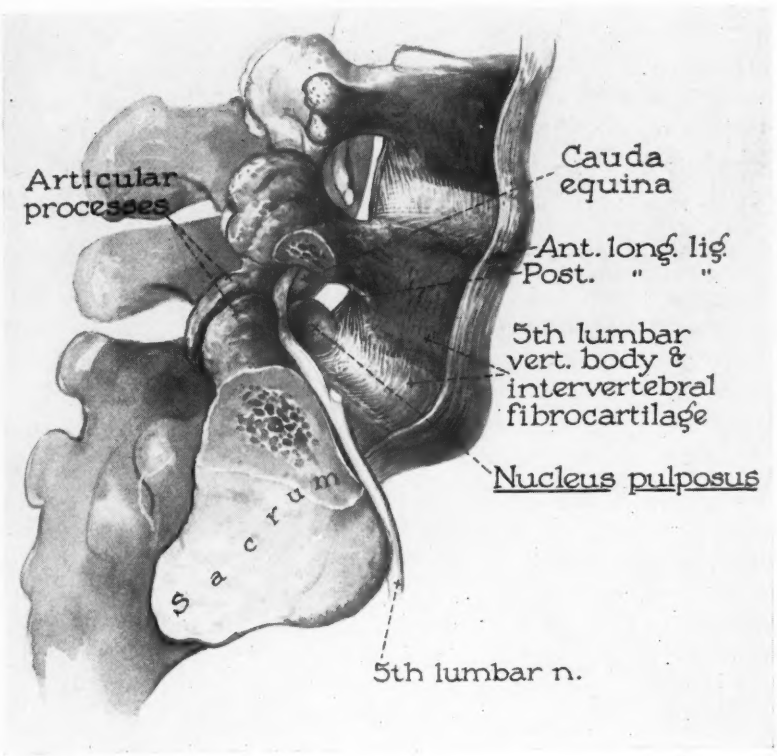
Articular processes
Cauda equina
Ant. long. lig.
Post. " "
5th lumbar vert. body & intervertebral fibrocartilage
Nucleus pulposus
Sacrum
5th lumbar n.

FIG. 1

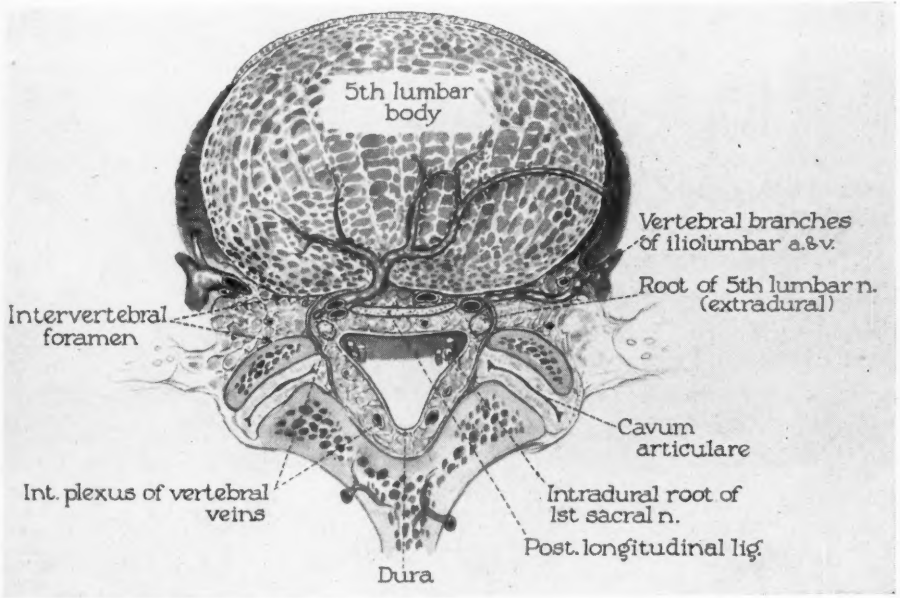
5th lumbar body
Vertebral branches of iliolumbar a.&v.
Root of 5th lumbar n. (extradural)
Intervertebral foramen
Cavum articulare
Int. plexus of vertebral veins
Intradural root of 1st sacral n.
Post. longitudinal lig.
Dura

FIG. 2

of the articular facets sliding up and down on each other, they slide from a posterior to an anterior position.

The angle of the joints may also vary on opposite sides. It is not infrequent to see in the same patient a perpendicular joint on one side and an oblique or horizontal joint on the other (tropism). In such a case the perpendicular joint will act as a pivot and the vertebra will rotate on the more or less horizontal joint, frequently producing pain in the more rigid perpendicular joint because of the rotary stresses.

The integrity of motion depends on many structures as well as upon the plane and angle of the joints. The interspinous ligament, the joint capsules, the ligamentum flavum and the posterior longitudinal ligament must maintain the relative position of stability unless the articular processes are properly formed to accept the downward and forward thrust of the weight of the body in the upright or flexed position. The muscles are called into play to support and produce motions which are willed by the patient. Any interference with function of any of these tissues, or any pathologic changes existing, can cause pain in the back which may be followed by radiation down the leg, depending on whether swelling or inflammation occurs around or near the exit of a nerve.

Anatomic study of a cross-section at the fifth lumbar vertebra shows that the fifth lumbar nerve usually makes its exit from the dura just above the level of the fourth lumbar disk. This is the rule in each vertebra above this point. The nerve passes downward and outward to enter the foramen. At the point of exit at the fifth lumbar foramen it is well below the disk. It lies immediately in front of the anterior part of the fifth lumbar inferior facet or lumbosacral articulation, just in front of the anterior part of the joint capsule. The posterior longitudinal ligament, which forms the anterior boundary of the neural canal, extends three-fourths of the way across the width of the canal. Entering the vertebra just lateral to the longitudinal ligament is an internal plexus of veins. The posterior longitudinal ligament is a fibrous structure and is one of the sturdiest parts of the annulus. It blends with the annulus and forms the posterior wall. The nucleus pulposus is situated just a little anterior to the posterior edge of the vertebral body (Fig. 3). The posterior and lateral wall of the neural canal is formed by the ligamentum flavum, which is attached to each vertebral arch above and below. The ligamentum flavum is cupped out at each intervertebral foramen where the nerves exit.

The measurements of these foramina in our specimens varied considerably. The average size was 7 Mm. from front to back in both the fourth and fifth lumbar openings. The measurement between the pedicles in the fourth lumbar averaged 19 Mm., and between the pedicles of the fifth lumbar, 12 Mm. The size of the ganglion in both the fourth and fifth lumbar vertebrae averaged about 7 Mm. (Fig. 4). It will be seen by these measurements in ten fresh specimens that the distance between the pedicles of the fifth lumbar is considerably narrower than in the fourth, and that the

diameter of the foramen is only slightly larger than the diameter of the ganglion. Inasmuch as the joint capsule and ligamentum flavum are continuous and almost inseparable by dissection at this point, it may readily be appreciated that any swelling or inflammation around the foramen could narrow the canal sufficiently to cause pressure upon the nerve root. Moreover, any inflammatory condition within the joint or any swelling or thickening of the ligamentum flavum in conjunction with the joint capsule could spread by continuity to the root of the nerve.

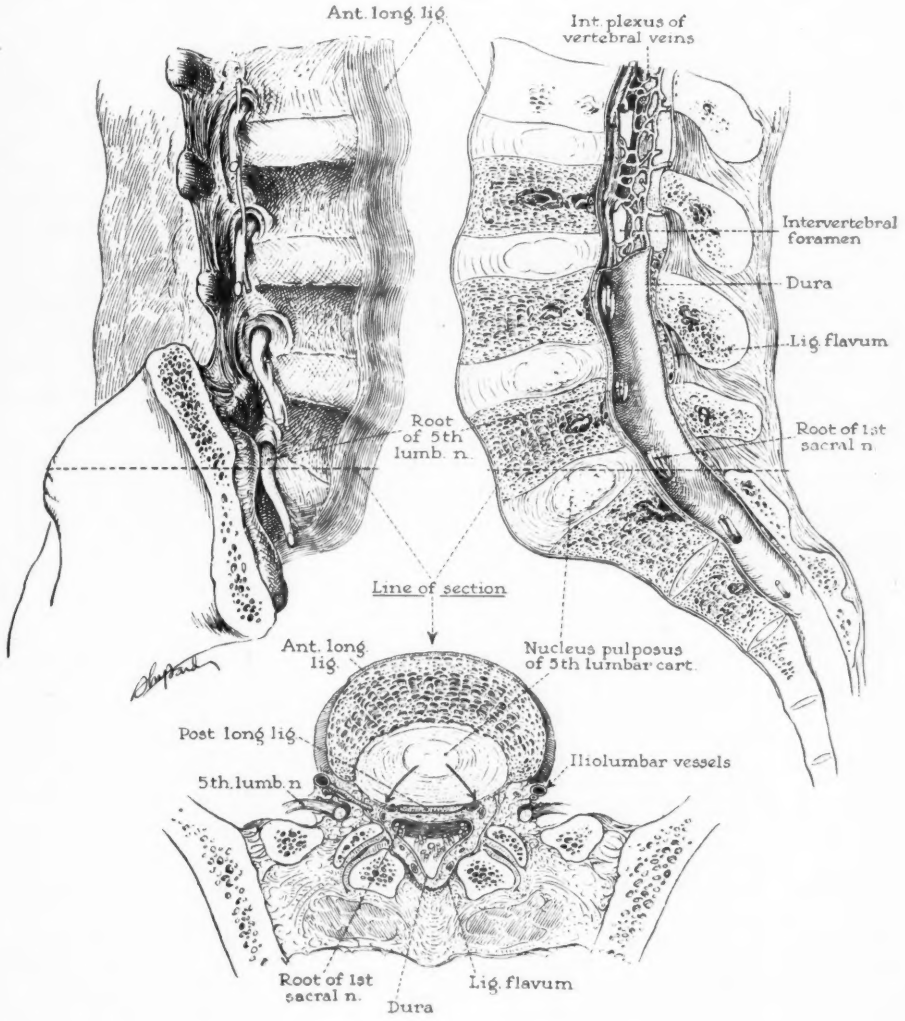

FIG. 3

Personally, I have never seen a case with pain referred to the sciatic distribution, disappearance of reflexes, or neurologic symptoms referable to interference with nerve function, appear in less than seven days after injury to the low spine, excepting in two instances where there was severe

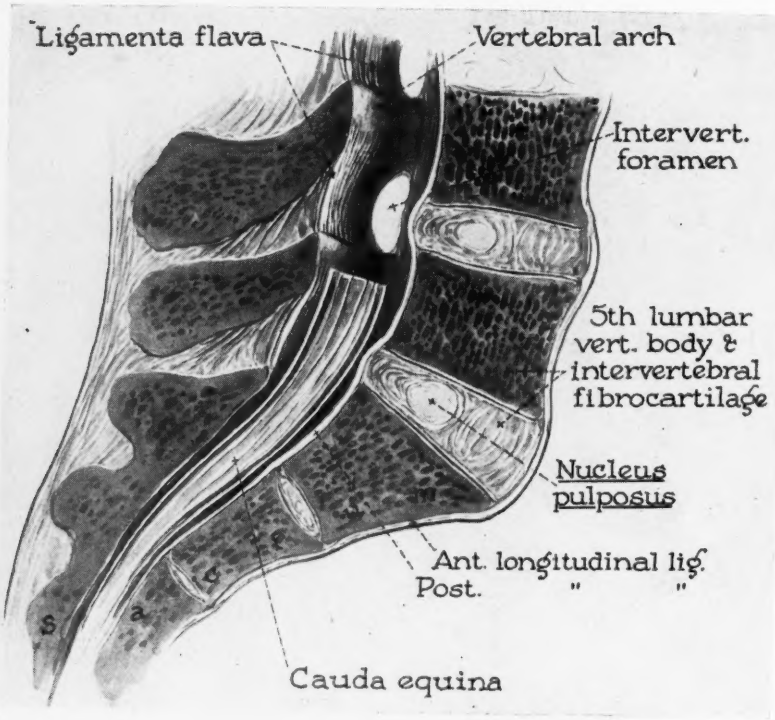
Ligamenta flava
Vertebral arch
Intervert. foramen
5th lumbar vert. body & intervertebral fibrocartilage
Nucleus pulposus
Ant. longitudinal lig.
Post. " "
Cauda equina

FIG. 4

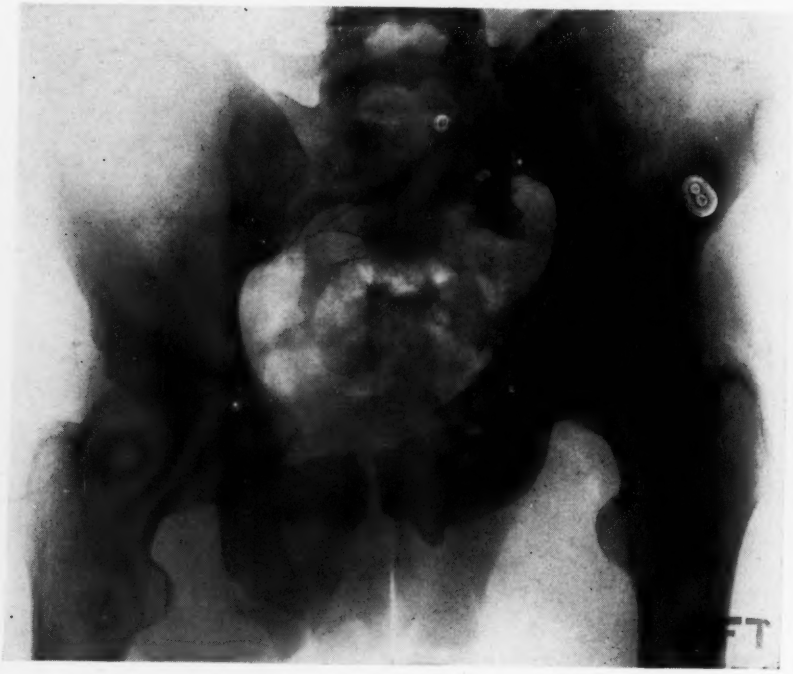

FIG. 5

injury (Fig. 5). In these two cases fracture and upward displacement of the ilium were present. Both patients had exactly the same symptoms referable to the sciatic nerve. I have seen similar symptoms many times in conjunction with low back pain where there was no roentgenologic evidence of pressure or injury to the nerve which exits from the low lumbar region.

In fresh specimens we were able to inject the capsule of the fourth and fifth lumbar joints and narrow the exit of the nerve by as much as 2 Mm. This narrowing was caused by mechanical distension and stretching of the capsule (Fig. 6). The injection was made with thorotrast in order to obviate any possibility of the material breaking through the capsule without roentgenologic evidence of such leakage. If it is possible to cause narrowing of 2 Mm. from simple pressure within the joint, it is quite evident that swelling within the joint, plus thickening of the capsule by inflammation and/or the ligamentum flavum, could cause narrowing of the foramen to a point where serious pressure might be exerted on the nerve. Schmorl[3] called attention to the fact that more than 15 per cent of his 10,000 cases showed degenerative process in the ligaments and tissues around the low spine, which means inelastic, thickened, hardened tissues.

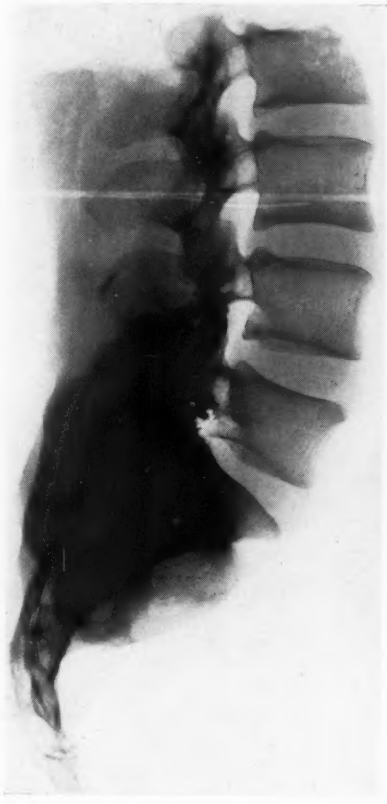

FIG. 6

We have previously demonstrated experimentally that arthritis with exostoses can be produced by trauma alone[4] (Fig. 7). This can be done repeatedly by weakening the support of a joint and causing it to bear cross-strain while the animal is active. Exostoses form around the edge of the joint and the cartilage degenerates progressively due to the often repeated slight traumata constantly administered to the weakly supported joint. These joints become roughened at the weight-bearing point, and this roughness extends toward the edges of the joint. The cartilage wears away at the point of greatest trauma and exostoses develop at the edge of the joint.

These pathologic changes are the same as are commonly seen in the spines of individuals who have done heavy work over a long period of time. When the joints become rough they do not glide normally. The rough margins serve as friction surfaces to the worn and degenerated cartilage.

This interference with smooth motion in the joint can cause catching and stabbing pain in the back, thereby creating muscle spasm and pain, exactly as seen in other joints similarly affected. We are all familiar with crepitation, thickening of the capsule, and swelling in the joints which can more easily be examined. There is no reason to suppose that the joints of the low lumbar spine differ in their pathologic reaction to various stimuli, such as trauma,

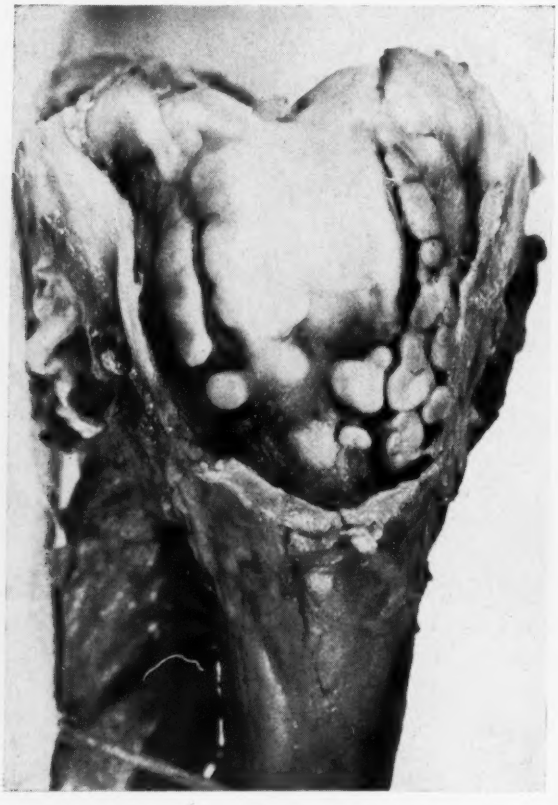

FIG. 7

infection, toxemia and allergic reaction. These may all be contributing causes in the degenerative process which occurs at an area well known to be a point of great mechanical stress. The degenerative process, when it occurs in a disk, may cause marked narrowing of intervertebral space, associated with collapse of the disk and irritation of the surrounding soft parts and bone (Fig. 8). When this happens, the annulus is pressed backward toward the canal and narrows the anteroposterior diameter of the canal. At the same time the foramen through which the nerve passes is diminished in size. Roentgenologic evidence of narrowing of the canal from front to back does not confirm the diagnosis of pressure on the canal or on its contents. That this irritation can be long-standing is shown in Figure 7 by the eburnation of the posterior lower third of the fifth lumbar vertebra. The area of osteosclerosis

is more marked at the posterior part of the body where the greater weight is borne. Although the fourth lumbar intervertebral space is somewhat decreased there is no sclerosis, because the weight is borne across the diameter of the bone. It is only at the point of greatest pressure that the most marked reaction is seen.

The anteroposterior diameter of the canal is ample to accommodate such increased bulging from in front without actual pressure on the contents.

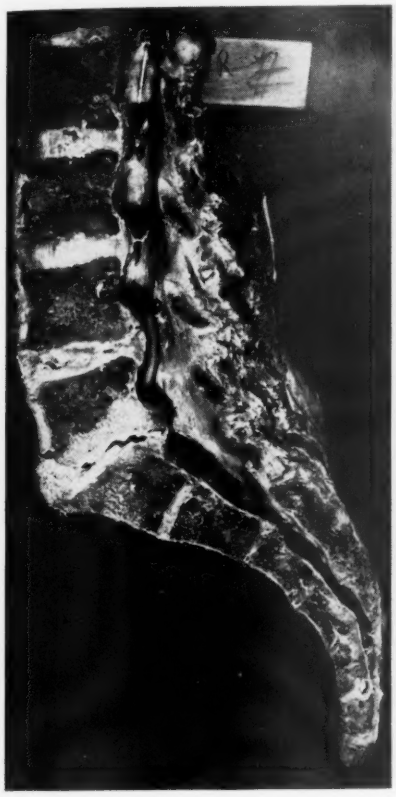

FIG. 8

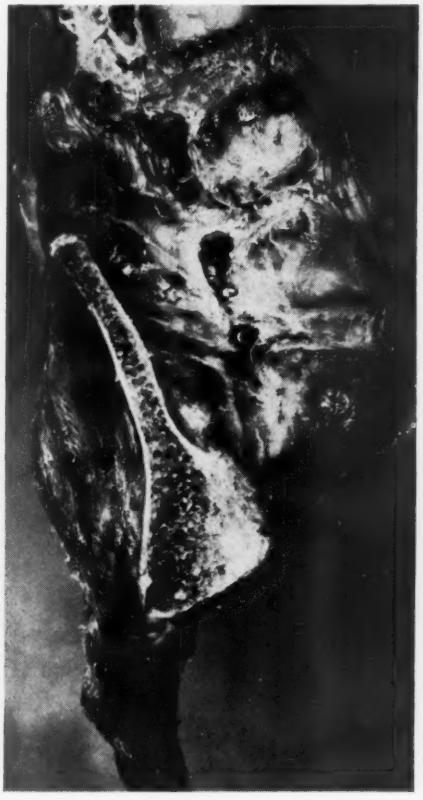

FIG. 9

The exits and course of the nerves through the foramen also vary. In one of the ten fresh specimens there was a double outlet laterally for the fifth lumbar nerve, the nerve dividing into two branches before it made its exit from the spine (Fig. 9). In another case the nerve divided just outside the ganglion; one branch passed through the foramen, the other ran down under a broad ligament to its exit one-half-inch below that of the upper branch. The lower exit was extremely narrow and the nerve was held firmly by the overlying broad ligament (Fig. 10-A). In another specimen (Fig. 10-B) the foramen was very narrow on the side of entrance of the nerve and widened at the exit, its perpendicular diameter being about one-half its anteroposterior diameter (Fig. 11).

It is quite apparent that variations in the path of the nerves are frequent not only in the foramen but at the exit from the foramen. Where the nerve is bound down, or the space through which it emerges is narrow, as in the specimens just described, a very little overstrain or inflammatory process in the ligaments through which the nerve makes its exit could cause definite

FIG. 10

symptoms of pressure on the involved branch. It is true that rupture of a nucleus pulposus could cause pressure upon a nerve where it leaves the dura and passes down to the vertebra below to gain entrance to the foramen. At this point the nerve is pressed into the corners of the triangular canal laterally. The nucleus is wedged between the root and the dura and presses the root toward the lateral surface of the canal, while the dura is pressed toward the median line (Fig. 12). If this happens the symptoms should be easily traceable to pressure upon this particular root, and there should be no question about its localization on physical examination. The reflexes should be interfered with and the pain should be referred to the area supplied by this root. The pain should be consistently localized to one place, and visual-

ization (of which I do not approve) should show a filling defect outside the dura (Fig. 13). If there is a rupture of the disk it can be plainly seen as a protruding mass outside the dura.

If it is necessary to make a crucial incision through the annulus in order to disclose the nucleus, then any existing symptoms are not due to a disk,

FIG. 11

FIG. 12

hidden or herniated. It is always possible through an incision in the annulus to curet or otherwise bring out the material which forms the disk. No incision should be made in the annulus at the time of exploration. If there is a hernia of the disk it lies on the anterior surface of the canal between the dura and the annulus through which it has ruptured; further exploration is unnecessary. Should the annulus be punctured by trauma which forces the disk out, or by an instrument at the time of operation, this causes collapse of the intervertebral space. If the center of the disk degenerates or is allowed to escape through rupture in the annulus, the remainder of the disk may be forced backward into the canal, as shown in Figure 8. Collapse of the disk with narrowing of the space between the vertebrae throws the articular facets between the vertebrae into a distorted position; the angle may be

changed or they may override. This, in itself, puts strain on the joints, the capsules and the supporting ligaments, and will eventually produce traumatic inflammatory reaction which will necessitate furnishing support for the joints.

It may be asked why a certain number of patients are relieved of pain when they are operated upon for ruptured nucleus pulposus when no rupture has been found, only to have, later, a recurrence of symptoms. It is my

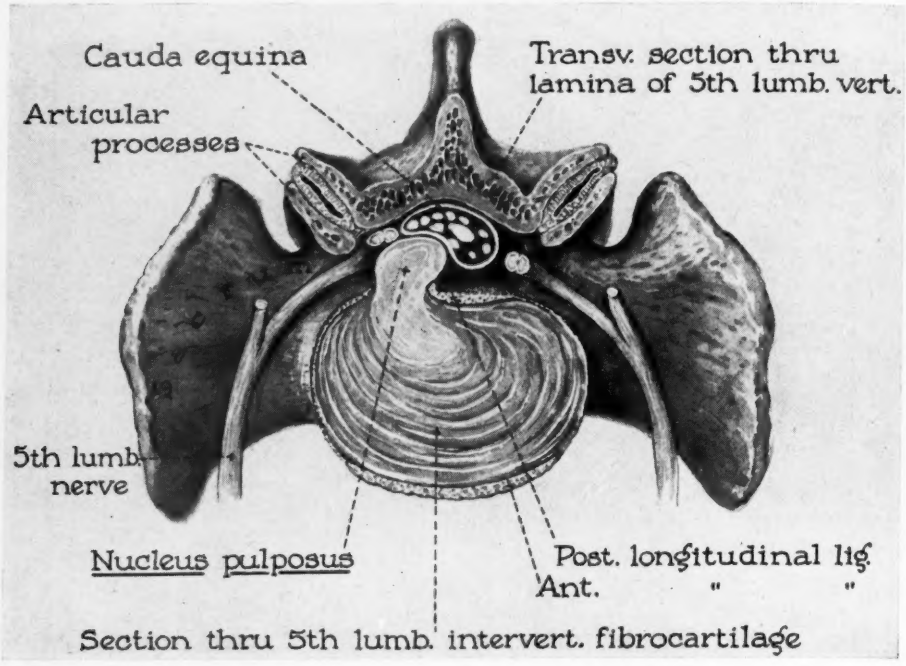

FIG. 13

opinion that the reason lies in the fact that part of the lamina and the ligamentum flavum is removed, resulting in decompression of the probably thick and indurated parts of the joint which is continuous with the ligamentum flavum. Also, in the manipulation of operative procedure, joints which are locked because of roughness, muscle spasm and inelasticity of the ligaments, are relieved. I have seen many patients recover from their symptoms following rest in bed with traction, without any surgical procedure.

It is my opinion, therefore, that the reason for onset of pain after injury to the low back is, in a large number of cases, intimately connected with strain or other injury to the low lumbar ligaments and joints, associated with swelling and inflammation which, in turn, may be caused by minor strains of ligaments or joints already somewhat degenerated, or by lack of mechanical bony support at this point because of malformation.

There are many other contributing factors which cannot be discussed in a communication of this kind because they are not directly related to the

subject matter with which we are concerned. It is sufficient to say that the low back can be, and frequently is, the site of sudden severe pain followed by sciatic pain in days, weeks or months, which may be due to a combination of physiologic degeneration of the supporting tissues, infection, toxemia, arthritis, or a combination of one or more. These cases should not be subjected to operation on suspicion; they should be thoroughly investigated and an attempt made to establish a diagnosis. A large percentage of these patients get well with rest and traction and adequate treatment of the systemic condition which is a contributing factor. The promiscuous operation for and removal of intervertebral disks without definite evidence of root pressure is not justifiable until every other method of treatment has been reasonably tried.

I believe the spine should be permanently immobilized at the time of operation for a ruptured nucleus pulposus, whether or not the rupture is found. If the symptoms have been severe enough and have persisted for a sufficient length of time to warrant operation for their relief, then permanent relief should be afforded the patient by taking the strain off the degenerated tissues at the point from which the pain emanates. This can be done only by permanent immobilization.

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AN ANATOMIC STUDY OF THE LUMBOSACRAL REGION IN RELATION TO LOW BACK PAIN AND SCIATICA

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FOR MANY YEARS the syndrome of low back pain with associated sciatic nerve radiation has been a subject for investigation. The complex anatomy of the lumbosacral and sacro-iliac regions, combined with numerous anatomic variations, has complicated the problem of etiology of this clinical entity.

Two etiologic factors are now generally accepted as the basis for low back pain and sciatica. It has been conclusively shown that pain may arise in the joints, ligaments and muscles of the lumbosacral region and be referred throughout the distribution of the sciatic nerve. Pain may also arise from compression or irritation of the sciatic nerve at its roots. This may occur in the spinal canal, in the intervertebral foramina where the nerve roots are in contact with the intervertebral joints, or along the course of the nerve after its exit from the spinal canal.

This latter factor of compression of the nerve components has, in recent years, been emphasized by the widespread advocation of the theory of herniation of the intervertebral disk into the spinal canal. It is a fact, however, that compression or irritation of the nerves may as readily take place in the intervertebral foramina where the nerve roots and ganglia are confined in a relatively smaller space. The anatomy and relationships of the sciatic nerve components to the structures composing the intervertebral foramina predispose to compression when pathologic changes occur in this region.

It was this fact which led us to take up the study of anatomic and pathologic changes in the lumbosacral joints and foramina. Ten unselected lumbosacral spines were obtained at autopsy, and dissected to determine the variations in anatomy and pathology which may affect the spinal nerves as they course through the foramina. The fourth and fifth lumbar intervertebral foramina were studied to determine: (1) The relative size of the nerves to the foramina; (2) the effect of swelling and effusion in the intervertebral joint capsules on the nerves and ganglia; and (3) the effect on the nerves of variations in ligamentous or osseous structures in the region of the foramina.

The fourth and fifth lumbar spinal nerves emerge obliquely from the spinal canal (Fig. 1). The nerve with its ganglion as it lies in the foramen is bounded above and below by the pedicles of the adjacent vertebrae, anteriorly by the body of the vertebra and intervertebral disk, posteriorly by the capsular ligamentum flavum. The capsular ligamentum flavum forms the

capsule and ligamentous support of the anterior portion of the intervertebral joints.

Measurements were made of the fourth and fifth lumbar foramina and the respective nerves, to determine the relative size of each. The diameter measured between the vertebral pedicles was found to average 12 Mm. in the fifth lumbar foramen and 19 Mm. in the fourth. The largest diameter measured between the capsular ligamentum flavum posterior and the vertebral body anterior averaged 7 Mm. in the fourth and fifth foramina.

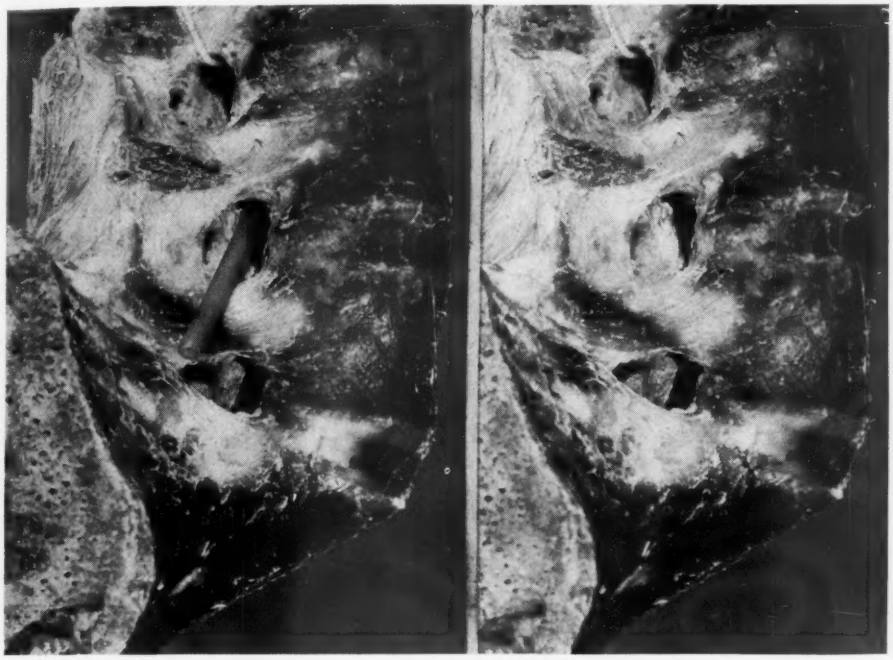


FIG. 1 FIG. 2

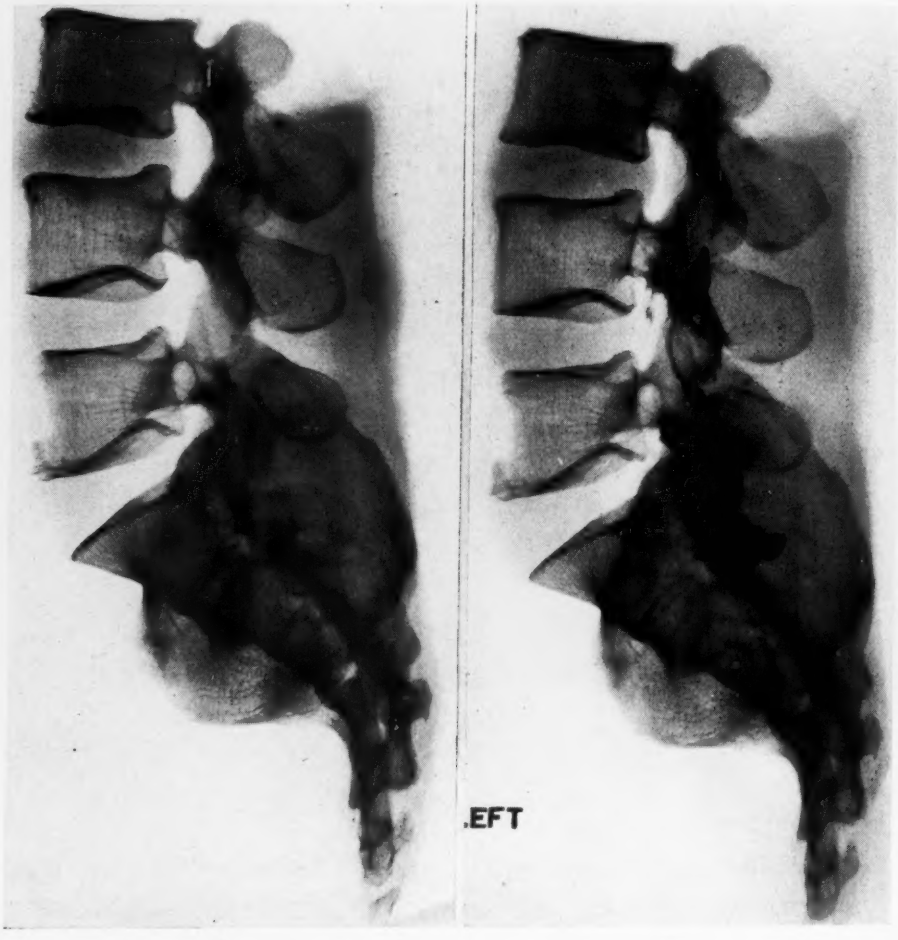
FIG. 1.—Illustrates the oblique course of the spinal nerve through the fourth lumbar foramen, as represented by rubber tubing inserted; and shows the relationship of the nerve to the capsular ligamentum flavum.

FIG. 2.—Swelling occurring in the capsular ligamentum flavum in the fourth and fifth lumbar foramina following injection.

Comparing the average size of the fourth and fifth nerves, which measured a fraction of a millimeter less than 7 Mm. to the average anteroposterior diameter of the foramina, which measured 7 Mm., one is impressed by the intimate relationship of the nerve to the foramen. It may be concluded from these measurements that moderate swelling of the capsular ligamentum flavum can cause compression of the nerve in the foramen.

To determine the degree of distention or swelling of the intervertebral joint capsule necessary to compress the spinal nerves, the joint capsules of the fourth and fifth lumbar joints were injected with radiopaque oil under pressure. Roentgenograms were made and measurements of the foramina were repeated.

Figure 2 illustrates the point where swelling of the capsular ligamentum flavum was most marked. The anteroposterior diameter of the foramina was reduced from an average of 7 Mm. to an average of 5 Mm. in the 40 joints injected. Roentgenograms made before and after injection clearly show the distention of the joint capsule and protrusion of the ligamentum flavum into the foramen (Fig. 3). This distention took place regularly at a point intimately in contact with the ganglion of the spinal nerve.



A B

FIG. 3.—A and B: Demonstration of radiopaque oil producing protrusion of the joint capsule into the fifth lumbar foramen: before and after injection.

Many anatomic variations have been reported in the lumbosacral region. In our series of spines a number of anatomic and pathologic variations were found. Four main pathologic processes were noted which produced compression of the spinal nerves in the intervertebral foramina or of closely related structures: (1) Posterior lipping or spur formation of the vertebral bodies at the foramen; (2) anomalies of the vertebral bodies, particularly

the first sacral; (3) degeneration of the disk substance, with collapse of the intervertebral space; and (4) variations in the ligamentous structures at the exit of the nerves from the spine.

Posterior lipping of the fifth lumbar vertebra occurred in four specimens. In each case the osteophyte formations were located in the foramina and produced narrowing of the anteroposterior diameter. All cases were associated with moderate to severe degenerative changes in the disk substance. Compression of the nerve was evident in two of the spines. (Refer to Magnuson's article, Fig. 8, p. 887.)

Anomalies of the first sacral vertebra were found in two spines. Spur formation on the posterior surface of the vertebra with impingement on the nerve at the exit from the foramen was noted in one case. A deep sulcus, formed by the body and transverse process of the first sacral vertebra, confined the fifth lumbar spinal nerve in the second case. The nerve was bent sharply at the point of exit from the foramen, and was bound tightly into the sulcus by firm ligamentous strands. Compression of the nerve in each case was only moderate. (Refer to Magnuson's article, Fig. 11, p. 889.)

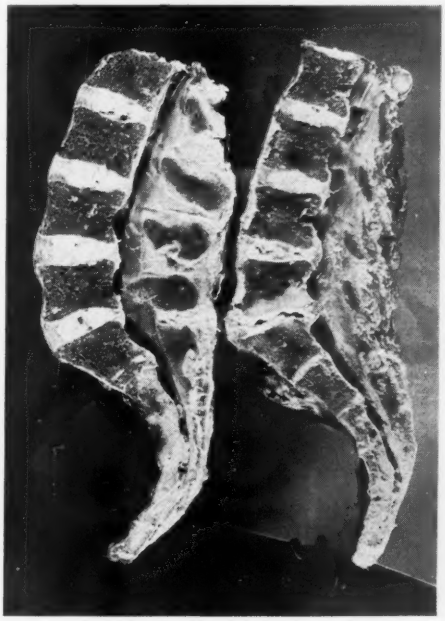


FIG. 4.—Comparison of normal vertebral canal and disks, with extreme degeneration of the disk and sclerosis of the vertebral bodies.

Degenerative changes in the disk substance between the fifth lumbar and the first sacral vertebrae (Fig. 4) were a prominent finding in this series of spines, occurring in four cases. Collapse of the intervertebral disk, without protrusion into the spinal canal, produced the most marked narrowing of the fifth lumbar foramen with compression of the nerve. Extreme sclerosis of the involved vertebral bodies with marginal lippings was a prominent feature in the pathology. Figure 9 of Magnuson's article, p. 887, illustrates the marked reduction in the size of the foramen that takes place with collapse of the disk substance, particularly the distance between the pedicles.

The ligaments which join the fifth lumbar vertebra with the first sacral vertebra are subject to great variation, as was confirmed by our series of spines. In three cases it was noted that one ligament connected the transverse process of the fifth with the body of the fifth and the first sacral vertebrae. This ligament lay directly over the intervertebral foramen at the exit of the fifth lumbar nerve. The extent to which the ligament was

developed varied considerably. (Refer to Magnuson's article, Fig. 10, p. 888.) The ligaments in each case bound the nerve firmly to the body of the first sacral vertebra. Evidence of compression could not be demonstrated in the two similar cases.

Numerous other changes were found in this series of unselected spines, including advanced arthritic changes in the articular facets, anomalous facets, variations in the angle of articulation of the fifth lumbar and first sacral vertebrae, and irregularities of the contour of the spinal canal. None of these anatomic variations produced compression of the spinal nerves.

It is of interest to note that although advanced degeneration of the disk substance was present in four cases, there was no rupture of the annulus fibrosus with protrusion of the disk into the canal. Compression of the cauda equina was not demonstrated in any specimen.

SUMMARY

A series of ten unpreserved autopsy spines were dissected to determine the factors which may produce compression or irritation of the spinal nerves in the intervertebral foramina.

By injection of oil into the joints of the fourth and fifth lumbar vertebrae, sufficient swelling was produced in the capsular ligamentum flavum to compress the spinal nerves in the foramina.

Four anatomic and pathologic factors produced compression of the spinal nerves in the spines of this series: (1) Posterior lipping of the vertebral bodies; (2) anomalies of the first sacral body; (3) narrowing of the intervertebral foramen due to collapse of the disk; and (4) variations in ligamentous structures adjacent to the fifth lumbar foramen.

CHRONIC SPINAL EPIDURAL GRANULOMA*

REPORT OF TWO CASES

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CHRONIC SPINAL EPIDURAL GRANULOMA is a condition that occurs infrequently and is associated with acute epidural spinal abscesses, for both may have a common etiology. There were only 88 of these cases reported between 1855 to 1937, as reviewed in the literature by Ira Cohen,[1] in 1938. At that time he reported seven cases, five of acute epidural suppuration, and two of granulomata. Watts and Mixter,[2] in 1931, reported four cases of chronic spinal epidural granulomata. No definite etiologic factors have been established in the cases of chronic spinal granuloma, tuberculosis and syphilis excluded, but certain conditions have existed in the body prior to the onset of neurologic findings of cord compression. These various conditions include a carbuncle of the neck, sepsis of the hand, traumatic back injury, perirectal infection, and convalescence from typhoid fever. In other cases no history of infection was ever present.

We are reporting two cases of chronic spinal epidural granuloma. In the first case there was a history of a draining perirenal abscess which had existed one and one-half years before the onset of the symptoms of spinal cord involvement. There was no other history of illness for many years which could account for the findings at operation. Extension of pus from the kidney to the thoracic spinal cord probably was by lymphogenous or hematogenous route.

In the second case, the patient was operated upon at this hospital for an osteomyelitis of the squamous portion of the right temporal bone. This condition came to Surgery, November 13, 1941, and the patient's first neurologic symptoms were noticed April 19, 1943, a time interval of about one and one-half years. The patient stated that he had been perfectly well during the year and one-half-period, and had suffered from no illnesses.

Case 1.—L. M. B., male, age 47, was admitted to the Neurologic Service, November 23, 1942, with a tentative diagnosis of spinal cord tumor or multiple sclerosis. He gave a history of having a perinephritic abscess in 1938, which drained for two or three months, and from which he had fully recovered. His first neurologic symptoms were low dorsal back pain with costal radiation, exaggerated by coughing and sneezing,

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which began in April, 1940. There was no evidence of sepsis at this time. The patient was then treated with short-wave therapy to the back, and his pain disappeared after three months treatment. In August, 1940, the patient noticed that he had trouble in keeping his footing while walking on rough ground or going up stairs. He gradually developed weakness of both lower extremities and tendency to a spastic gait. He was admitted to another hospital in September, 1940. At that time the neurologic findings showed a sensory level at about the 10th dorsal segment. The deep reflexes in the legs were increased and the Romberg sign was positive. Queckenstedt's test was positive for a complete subarachnoid block. Lipiodol visualization of the spinal cord revealed an extensive filling defect at the 12th dorsal vertebra. A laminectomy was performed at this level, and no gross pathology of the cord or vertebra was found. A tumor higher in the thoracic region was suspected because of the sensory level. Under fluoroscopic examination, and in the Trendelenburg position, the lipiodol ran freely through the subarachnoid space into the cervical region. It was the opinion of the neurosurgeon that a tumor of the higher thoracic region was not present because of an absence of obstruction. The patient was later seen by a neurologist, and a gastric analysis taken with histamine revealed an absence of free hydrochloric acid. The blood picture was essentially normal.

The patient was put on thiamine chloride hypodermically and orally, given massive doses of reticulogen, and dilute hydrochloric acid, as well as a high protein and high vitamin diet. He responded rather well; however, he still had some weakness of the lower extremities. The impression at this time was that the patient had a multiple sclerosis. There was no bladder disturbance noted, but the patient did have some loss of erection. In December, 1940, the patient caught a cold and he noticed the weakness of the lower extremities to be more marked. He was again examined. The gastric achylia was again found, with a normal blood picture. The patient was given liver extract intramuscularly; thiamine chloride hypodermically and orally; and quinine, grains five, three times a day. He responded very well at this time to this regimen so that, in March, 1941, he was able to return to his legal work and was walking with no discomfort or weakness of the extremities. The patient stopped his medication of his own volition at the end of 1941. In March, 1942, he noticed that he was experiencing difficulty in walking and that his feet felt heavy. He resorted to his former therapy, but there was no response this time, and he was soon confined to a wheel-chair. In April, 1942, he had a complete paraplegia of his lower extremities. He entered our hospital November 23, 1942, and, on examination, it was found he had a complete paralysis of the lower extremities and of the trunk below the level of the 10th dorsal segment, shown by positive Beevor's sign. Occasionally, on passive movement a localized hypertonicity occurred in the lower extremities, hyperextension of the great toes, and an involuntary flexion of the legs. At other times there was no great hypertonicity. The Achilles jerks were obtainable and were about equal, perhaps the right a little greater than the left. The same was true of the knee jerks. There was no ankle clonus and no knee clonus. There was no motor disturbance in the upper extremities and the reflexes were normal. The plantar reflexes were absent, as well as the cremasterics and abdominals. No pathologic reflexes could be elicited. There was loss of sensation to touch at about the level of the 8th dorsal segment, a little higher on the right than on the left side. On the left side the diminution to all the sensations of heat, cold and pain were less over the sacral areas than any other area. The motor cranial nerves were normal and fundoscopic examination was negative. Queckenstedt's test was positive again. Examination of the spinal fluid was as follows: Clear and colorless, positive Ross-Jones, nine cells per cm., Wassermann negative, and the Lange colloidal gold curve 0000112212. Total protein 65 mg. Gastric achylia was present, with a normal blood picture. There was no tenderness of the spine over the dorsal vertebrae. The impression was that the patient had a transverse lesion of the spinal cord extending

up to the level of the 6th dorsal vertebra, probably due to compression, and a laminectomy was indicated.

Operation.—January 27, 1943: Laminectomy disclosed beneath the thoracic vertebrae (6th, 7th, 8th, 9th and 10th) a dense mass of tissue encircling the dura on its dorsal and lateral aspects. It was fibrous and very adherent to the cord, and had to be removed with the ronguers, using considerable force. The tissue was avascular, and when the dura was opened the exposed spinal cord was devoid of some of the blood supply and appeared yellowish-gray rather than normal pinkish-gray in color. A catheter, passed from eight to ten centimeters superiorly and inferiorly from the operative field in the subdural space, met with no interference.

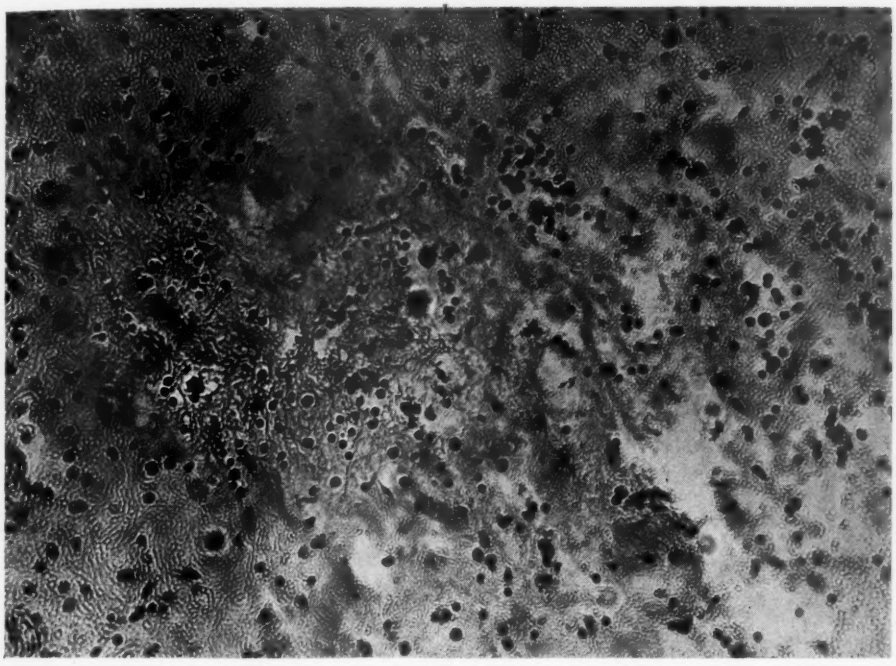

FIG. 1.—Case 1: Section from extradural mass. Note chronic inflammatory tissue with diffuse round cell infiltration and occasional giant cell. (× 300)

Pathologic Examination: Sections of the material submitted revealed an organized, inflammatory exudate, in most instances completely organized and fibrosed. There was much granulation tissue made up of newly-formed blood vessels and inflammatory cells of all types, round cells and mononuclear cells predominating; there were a few polymorphonuclear cells. There were large masses of macrophage cells containing pigment and débris. A dense scar surrounded these areas. *Pathologic Diagnosis:* Organized and fibrosed inflammatory tissue.

Three or four days after the second laminectomy, the patient began to move his toes and flex his ankles, slightly. Physiotherapy management was instituted ten days following surgery, and within two weeks the patient was able to lift both legs from a sitting position. Two months after discharge from the hospital the patient wrote that he was able to walk with the use of a cane and could walk up and down the stairs. Recently, the patient visited us at the hospital, and his gait was almost normal.

Case 2.—R. E. L., male, age 65, was readmitted to our Neurologic Service, August 5, 1943, with a tentative diagnosis of spinal cord tumor. He gave a history of having been operated upon here, November 13, 1941, for osteomyelitis of the skull, involving

the posterosuperior portion of the squamous part of the right temporal bone. A stitch abscess delayed the healing of the wound for a few weeks but it was completely healed when the patient was discharged from the hospital. He was asymptomatic until April, 1943, when he began to notice some weakness in the lower extremities, associated with paresthesia. He had low dorsal back pain with costal radiation. He entered a private hospital, in July, 1943, and remained there for three weeks. During this period of hospitalization his legs became weaker, until he became totally paralyzed in the lower extremities. He had loss of sphincter control of the bladder and rectum.

Physical Examination: It was found that he had a complete paralysis of both lower extremities. There was a loss of sensation to touch slightly above the nipple on the left side and just below the nipple on the right. A complete flaccid paraplegia was present, with loss of all forms of sensation, including deep pressure pain in the lower extremities. The Babinski sign was negative, bilaterally. The patient had an indwelling catheter, and had a large decubitus ulcer in the sacral region. The motor cranial nerves were normal, and fundiscopic examination was negative. Spinal fluid examination revealed a complete subarachnoid block with a total protein content of 120 mg. The fluid was xanthrochromic, globulin was 4-plus Ross-Jones, ten cells per cm. Wassermann was negative and the Lange colloidal gold curve was 0000123332. There was no tenderness of the spine over the dorsal vertebrae. The impression was that the patient had a tumor of the spinal cord at the level of the 4th dorsal vertebra. However, since admission, the patient had been passing tarry stools, and laboratory examinations were positive for occult blood and occasional blood cells. The patient admitted being given charcoal for a supposed stomach disorder prior to admission to the hospital; however, examinations, to rule out a malignancy, were completed, and roentgenograms of the spine, skull, chest, pelvis and G. I. series were negative. The patient took a turn for the worse and, on September 10, 1943, he became critically ill, and died September 17, 1943, no surgery having been undertaken.

Autopsy.—Longitudinal section of the dura disclosed several irregular areas of thickening and fibrosis of the dura at the level of the 4th to the 6th dorsal spine. The thickenings were in close apposition to the spinal cord, and resulted in compression of the cord itself. Section of the spinal cord produced an exudation of gelatinous, yellowish-white material from the parenchyma of the spinal cord. There was evidence of pressure liquefaction necrosis of the nervous tissue of the spinal cord.

Pathologic Examination.—Microscopic: This revealed a granulomatous process with extensive fibrosis. There was diffuse infiltration of all types of leukocytes, round cells, plasma cells, eosinophils, mononuclear cells and an occasional giant cell. The reaction was quite diffuse, although in some areas there were aggregations around the blood vessels. There were no definite tubercles noted, and none of the specific yeast fungus organisms could be seen. The lesion is apparently nonspecific, and was, apparently, that of chronic inflammatory granulomatous tissue.

DISCUSSION

The diagnosis and treatment of chronic spinal epidural granuloma is like that of any spinal cord tumor. One finds spinal cord compression symptoms and signs; increase of lymphocytes and protein in the spinal fluid in some cases; partial or complete spinal block; occasional tenderness over the spine in early cases; and the Lange colloidal gold curve indicative of some pathologic process, but not characteristic. Loss of early sphincter control may occur in some cases, while in others loss of erection may be manifested. Exaggerated tendon reflexes in the legs, ankle clonus, and Babinski signs have been found present. Lipiodol visualizations show a definite block in

some cases. At our hospital this procedure is not used, Davis, Haven and Stone[3] stating that the use of lipiodol may cause an arachnoiditis of the spinal cord. In the first case reported, lipiodol examination was completed prior to the patient's admission to our hospital. It revealed an extensive filling defect at the 12th dorsal vertebra. Laminectomy had been performed elsewhere at this level, but no gross pathology of the cord or vertebra was found. Sensory level, however, at about the level of the 8th dorsal segment was present and indicated a transverse lesion of the spinal cord extending up to the level of the 6th dorsal vertebra, probably due to compression; however, the examiner was misled by the lipiodol running freely through the subarachnoid space when the patient was placed in the Trendelenburg position. We feel that a permanent sensory level is satisfactory neurologic evidence of cord compression, without the additional use of lipiodol visualization.

In the first case the presence of an achylia associated with the neurologic picture was probably incidental, the blood picture being normal. The patient responded well to liver extract and thiamine chloride and quinine, but when repeated, a year later, it had no effect on the patient's condition. He became completely paraplegic.

The time interval of the complete paraplegia to surgical intervention was from April, 1942, to January 27, 1943. The first neurologic symptoms began in April, 1940. Hence, it was during a three-year period that the patient's pathologic process was present in the spinal cord. The results following surgery were quite remarkable, considering the time interval that the pathologic process was present, and the presence of complete paraplegia for nine months. Of the majority of cases reported, surgical intervention has been completed within three to six months from the onset of the first neurologic symptoms, and results have been very good; however, epidural granulomata can be present for a period up to three years, and surgery can still benefit the patient.

Although epidural spinal granulomata are not common, neurologists and neurosurgeons should bear in mind that they do occur. All cases previously diagnosed as spinal cord tumors should have a careful history for any antecedent infection occurring in the body prior to the occurrence of the first neurologic symptoms. A probable diagnosis of chronic spinal epidural granuloma can sometimes be made, and the prognosis, then, as far as recovery from surgery is concerned, can be considered good.

CONCLUSIONS

Two cases of chronic, spinal epidural granuloma are reported. In the first case good results were obtained from surgery despite extensive involvement of the spinal cord by granulomatous tissue extending from the 6th to the 10th thoracic vertebrae inclusively. The second case was not operated upon, due to the patient's poor condition. A draining perirenal abscess and an osteomyelitis of the right temporal bone of the skull, each occurring one and one-half years before the onset of the first neurologic symptoms of spinal

cord compression, can be considered as probable etiologic factors in these cases of chronic spinal epidural granulomata. Achylia with normal blood picture was an incidental finding in the first case. Lipiodol visualization can be misleading in the diagnosis of spinal epidural granuloma. The presence of a sensory level, although not equal on both sides of the body, is very suggestive of cord compression. Even though a chronic granuloma of the spinal canal has been present for three years, results from surgical removal can be quite successful.

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VENOGRAPHY: ITS VALUE IN THE DIAGNOSIS AND MANAGEMENT OF VENOUS DISTURBANCES OF THE LOWER EXTREMITIES

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THE NUMEROUS CLINICAL PROBLEMS originating in venous disturbances of the lower extremities have made venography a frequent and valuable aid in our work at McCaw General Hospital. Cases requiring further diagnostic investigation, and those cases which have been previously treated at other hospitals, with the results deemed not suitable for return to duty, are eventually sent to a general hospital for final disposition. During the past eight months, a surprisingly large number of interesting venous conditions of the lower extremities have been encountered and studied with the aid of venography. It is our purpose to present the characteristic features of the clinical case-groups encountered and to demonstrate their diagnostic and therapeutic significance.

The intra-arterial injection of sodium iodide for radiographic visualization of the main and collateral vessels was originally employed and described by Dr. Barney Brooks, in 1924. In recent years a fairly large group of investigators have contributed to the elaboration of venographic technic, the proper interpretation, and the applicability to the diagnosis and treatment of disease originating in the veins of the lower extremities. The technic which we have used is essentially that described in a previous publication, with some simplification and modifications adopted as the result of an increasing experience.

TECHNIC

The patient is placed in the prone position on a Bucky table, with the limb extended, moderately abducted and the foot everted. The patient should be placed so that the leg lies approximately along the midline of the table. Under local anesthesia, a vertical incision 1.5 cm. in length, is made about one centimeter posterior to the external malleolus. At this point a small terminal tributary of the external saphenous vein is readily isolated. A No. 19 transfusion cannula is tied into the vein. The three films, size 14 x 17 inches, are then placed in the following manner:

Film No. 1, wrapped in black paper only (not in a film exposure holder or cassette), is placed underneath the lower leg, its upper border slightly above the knee joint.

Film No. 2, wrapped in black paper only, is placed underneath the upper leg—films Nos. 1 and 2 should overlap for about two inches above the knee.

Film No. 3 is placed in a cassette in the Bucky tray, its center about underneath the hip socket. Films Nos. 2 and 3 should overlap considerably at the upper thigh.

The tube is elevated as far as the tube-stand permits (42 inches in our equipment). In a darkened room, with the filament lighted, the centration is so arranged as to cover all three films. A Luer-Lok syringe containing 30 cc. of 35 per cent diodrast solution is attached to the cannula and 1 cc. of solution is injected. If no major reaction is observed after a 15-second interval, the remaining 29 cc. are injected during a period of 45 seconds. Immediately upon termination of injection, one exposure is made covering all three films. This technic will prove satisfactory in most cases.

In the case of very tall patients or where visualization of the external iliac vein is particularly desired, the following modification is recommended: The tube is centered so that both proximal films are well covered, and this position checked by an adhesive marker or a rider on the rail. The tube stand is now moved distally and a cone inserted, and centration so arranged as to cover the most distal film only. The upper two films are protected through the cone. The injection of the contrast fluid is now started and, after 15 cc. have been injected, the film of the lower leg is exposed. The tube stand is then moved to its previously marked cranial position, the distal film and the cone are removed, while the injection of the contrast solution is continued. The exposure of the two remaining films is made upon termination of the injection.

The exposure data on our equipment (4-valve fully rectified Keleket unit) using technic No. 1 are: 100 Ma., 80 to 82 K.V., 8/10 to 1 second for the average patient. Using technic No. 2, modify as follows: 100 Ma., 78 to 80 K.V., 9/10 second for the lower leg, and about 82 K.V., 8/10 to 1 second for the upper leg and pelvis.

The considerable difference in the thickness of the limb over the calf and over the pelvic region is compensated for by the fact that intensifying screens are used over the pelvis while over the lower thigh and calf a non-screen technic is used. The films, simply wrapped in black paper, overlapping the film in the Bucky tray, do not interfere with proper exposure of the latter.

Fluoroscopic examination has been combined with radiography in the earlier studies. By increasing familiarity with roentgenologic technic and interpretation, the roentgenograms alone have proven satisfactory. Despite the fact that in many instances injections can be made directly into one of the dorsal veins of the foot or the distal end of the great saphenous vein, we have continued to use the "cut-down" procedure on the terminal branch of the short saphenous vein, in view of the fact that the tying of a cannula into the vein permits control at all times of the rate of injection and the positioning of the limb.

Despite the fact that we have encountered some variables in the pattern, we believe that the major features of the superficial, deep communicating veins and tributaries can be accurately determined under the constancy of

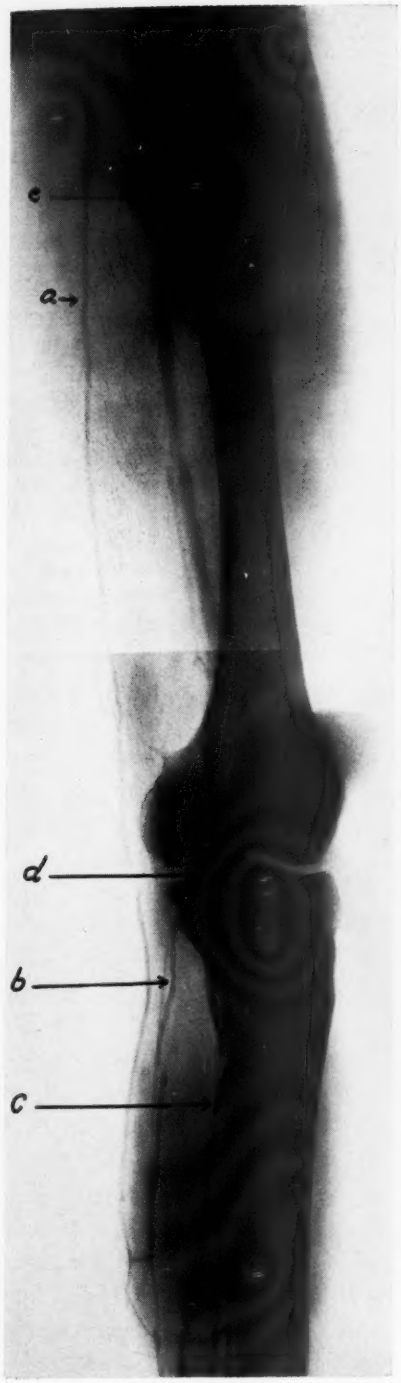

FIG. 1.—Normal Venogram: (a) Great (internal) saphenous vein. (b) Short (external) saphenous vein. (c) Deep veins of lower leg. (d) Popliteal vein. (e) Femoral vein.

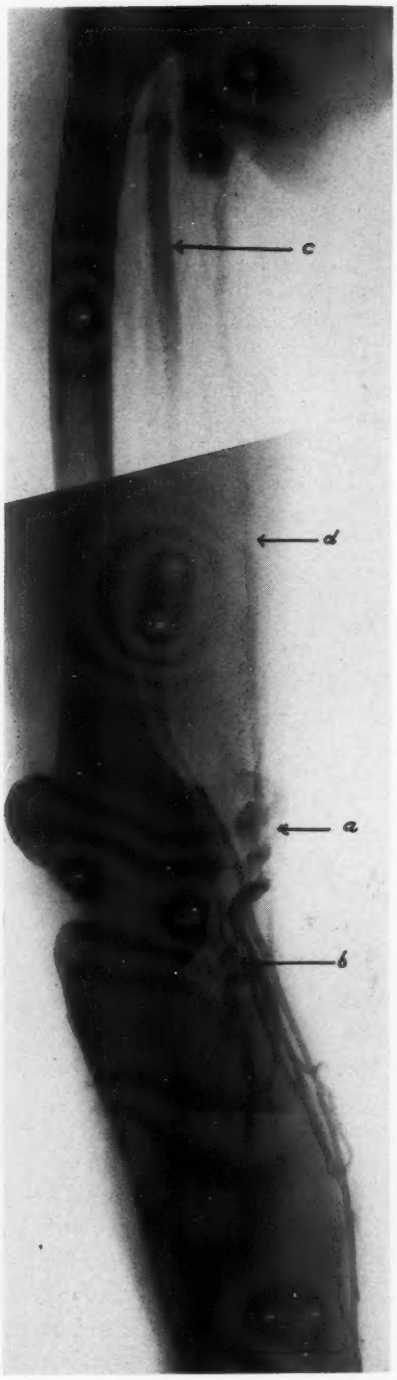

FIG. 2.—Cauliflower-like localized dilatation of communicating vein in typical location at the inner aspect of the knee (a), associated with severe varicose veins of the lower leg (b). Normal straight femoral vein (c). Patent straight great saphenous vein (d).

procedure. We have, therefore, felt it unnecessary to use the application of a tourniquet to force the venous return into the deep channels.

Normal Filling and Roentgenographic Visualization of the venous channels of the lower limb is illustrated in Figure 1. The important features are as follows:

(1) The deep tributaries of the lower leg fuse to form the venae comites of the anterior and posterior tibial arteries; these venae comites, in turn, fuse to form the popliteal vein.

(2) There is straight tubular filling of the popliteal and femoral veins, the latter continuing in the inguinal region as the straight tubular iliac vein.

(3) The great saphenous vein carries return superficial venous drainage from the entire medial aspect of the extremity, finally emptying into the femoral vein at the fossa ovalis in the groin. The short external saphenous vein carries return superficial venous drainage from the outer aspect of the lower leg, and empties into the great saphenous vein in the popliteal region or directly into the popliteal vein.

(4) Communicating veins exist in variable number between the superficial saphenous system and the deep veins in both the lower leg and thigh. The direction of flow normally is from superficial to deep.

(5) Competency and prevention of reversal of flow in the communicating veins and superficial veins is maintained by valves (Figs. 15a and 15b), which may be seen at varying levels. If these valves are partially opened, one sees two fine lines converging to the center of the vein. External to these lines symmetrical bulges in the vein walls represent the paravalvular sinuses (Fig. 15c).

A possible variant in the superficial saphenous vein in the upper thigh region is that of replacement of a single great saphenous by duplication or triplication of the vessel in the thigh, the multiple vessels joining to form a single saphenous trunk just before entrance into the femoral vein at the fossa ovalis. This variant is well illustrated in Figure 3.

CLINICAL CASE-GROUPS

I—VARICOSE VEINS

At this General Hospital we have been confronted with problems of recurring or indefinite varicose vein pathology. These cases fall into two classes:

(a) Those cases which have been referred for further evaluation of deep vein status and their possible applicability to surgical ligation. It is generally agreed that in a fairly large percentage of cases the usual clinical tests for determination of the adequacy of the deep veins (Perthe's test, Trendelenburg test, Ochsner-Mahorner tests) are all too frequently inconclusive, particularly if the superficial varicosities are large, tortuous and more or less sclerotic. It is, however, our experience that the use of venography with demonstration of an adequate deep venous return has enabled us to determine more accurately the suitability of severe cases of varicose veins for surgical ligation. Furthermore, in these cases of extensive superficial varicosities, we have been able to visualize the presence of extensive, dilated communicating veins, which, unless properly obliterated, would be a possible cause for recurrence and recanalization of the varicosities. A common type of such a communication

is the so-called "cauliflower-like" dilatation of a communicating vein frequently encountered in the region of the inner aspect of the knee, and well demonstrated in Figure 2, and Figure 15 (f).

Case 1.—A 34-year-old 2nd Lieutenant, was referred for disposition from an overseas Station Hospital because of extensive varicosities of the right leg of about three years duration, with development of superficial ulcerations on the inner aspect of the leg during the past six months. The report from the Station Hospital stated that the clinical tests indicated incompetency of the deep vein return. On examination, the two ulcers present and the surrounding area of chronic dermatitis of the skin was rather characteristic of varicose vein pathology. The varicosities of the leg were very prominent, tortuous, and almost sclerotic. *On performance of the usual clinical tests for deep vein competency, the superficial varicosities did not empty satisfactorily. Venography was performed and indicated an adequate deep vein return* (Fig. 2). Surgical ligation was performed, including a large cauliflower-like communicating vein, with an excellent clinical result. The ulcers were healed in six weeks, and the officer has now been returned to full duty.

(b) Those cases which have been operated upon previously, with subsequent recurrence of varicosities and their complications. It is admitted that even under the most ideal conditions there is still a fairly high rate of recurrence after surgical ligation and retrograde sclerosis therapy. We have performed venographic examination in all such cases sent in because of recurrences, and in almost every case we are able to visualize a communicating vein, usually in the midthigh, which permitted "shunting" from the femoral vein to the lower segment of the great saphenous vein (Figs. 5 and 6), which apparently was responsible for recanalization of the saphenous and reestablishment of varicosities considered to have been obliterated. In one of these cases, one of these communicating veins in the lower leg had become widely dilated to "venous-laking" proportion, and had been responsible for recurrent breakdown of soft tissue and chronic ulceration (Fig. 4). It was a relatively simple procedure to surgically obliterate the faulty communicating vein, as demonstrated venographically, with excellent clinical results.

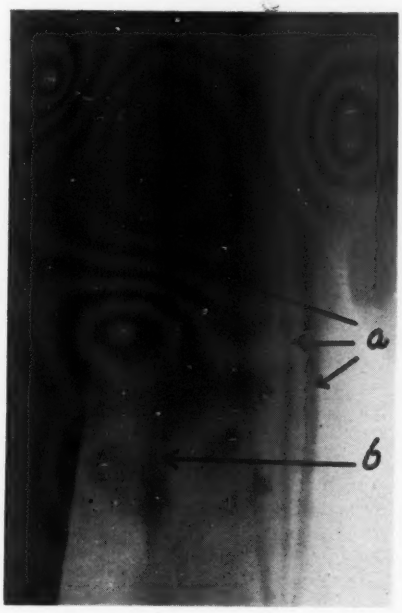

FIG. 3.—Normal Variant: Triplication of great saphenous vein (a). Femoral vein (b).

Case 2.—A 23-year-old Private, had been operated upon seven months previously, with high saphenous ligation and retrograde injection of sclerosing solution. He was admitted here with a complete recurrence of varicosities of the lower leg and considerable weeping dermatitis of the lower leg. Venography demonstrated a direct communication from the femoral vein to the saphenous vein at about the midthigh. Proximal to this point

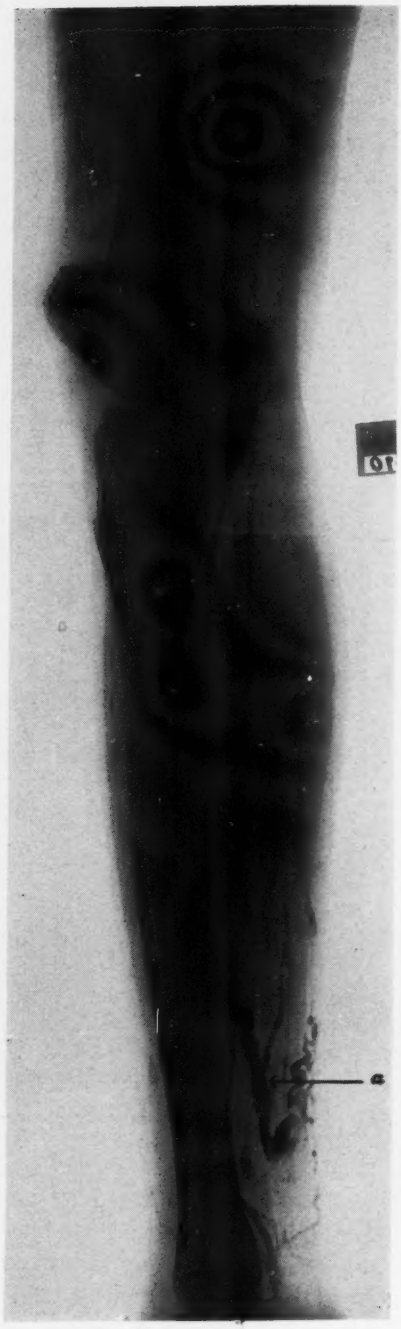

FIG. 4.—Surgical ligation of saphenous vein for varicose veins, with satisfactory obliteration of the saphenous vein, but failure to obtain cure. Large recurrent leg ulcer at the site of a markedly dilated, tortuous communicating vein (a) which had not been obliterated. Subsequent ligation of the communicating vein, revealed by venography, resulted in prompt healing of the ulcer.

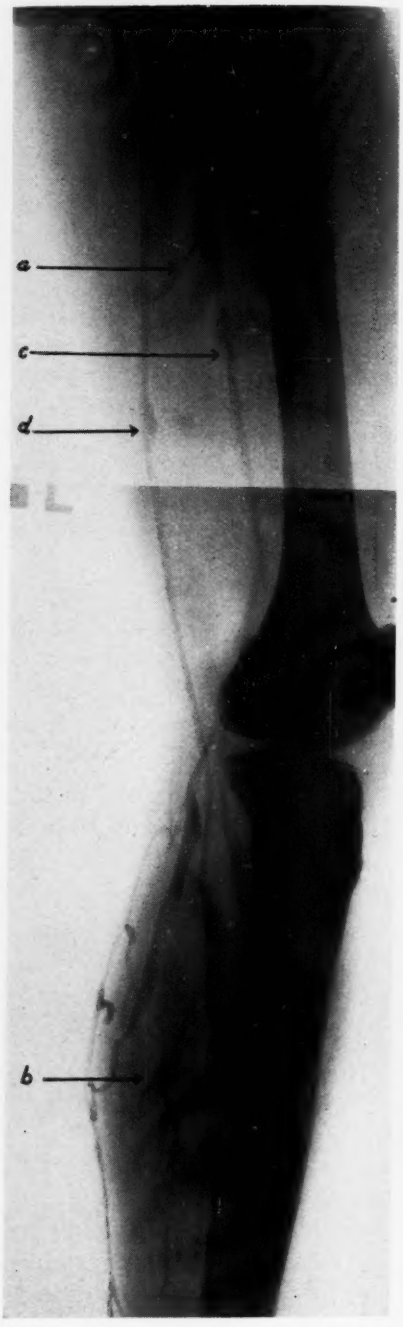

FIG. 5.—Recurrence of Varicose Veins Following Ligation of Great Saphenous Vein: Shunting of blood from femoral (c), to saphenous system (d), through a communicating branch (a) at the upper thigh. Varicosities (b) of the lower leg.

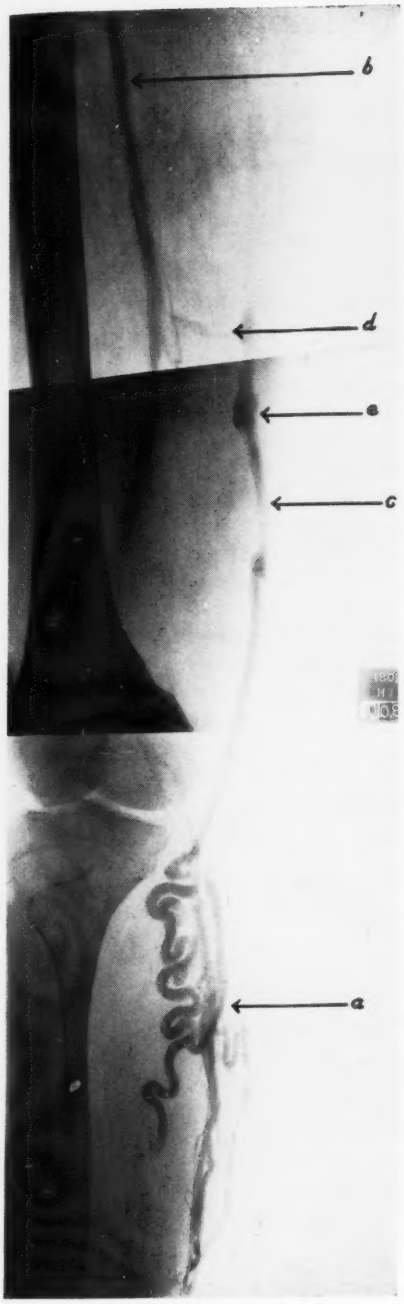

FIG. 6.—Recurrence of Varicose Veins (a) following Ligation of Great Saphenous Vein: Shunting of blood from femoral (b), to saphenous vein (c), through communicating vein (d) at the upper thigh. Paravalvular bulging because of overload (e).

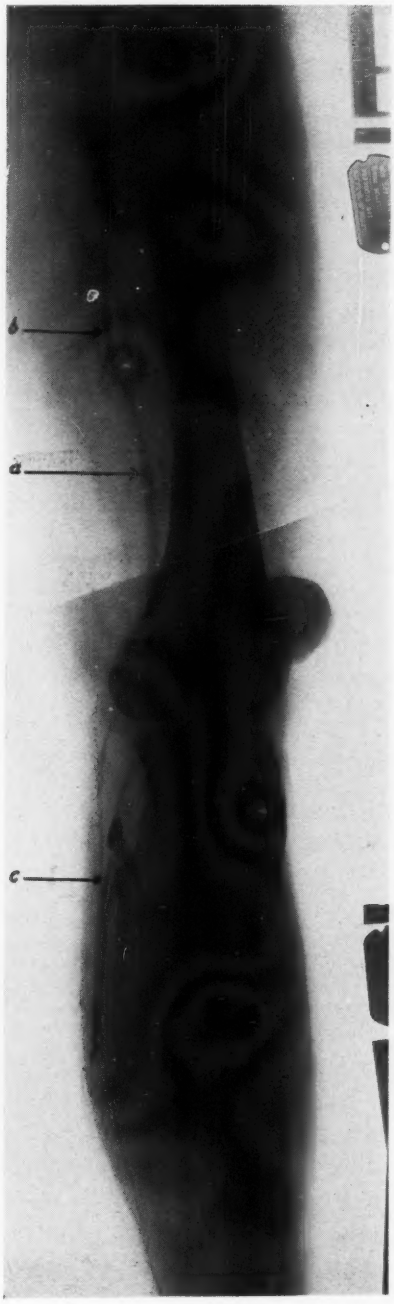

FIG. 7. — Superficial Thrombophlebitis (great saphenous vein not visualized): Femoral vein (a) patent, presents localized duplication (b). Varicosities of lower leg (c).

the saphenous had apparently been obliterated (Fig. 5). Reoperation was performed and the communicating vein obliterated by double ligation. Subsequent to operation, two injections of sodium morrhuate were made into the remaining varicosities of the lower leg. There was prompt obliteration of the varicosities and clearing of the skin manifestations of venous stasis. The patient was sent home on therapeutic furlough and was again observed on return, with no evidence of recurrence. The soldier has now been restored to full duty.

Case 3.—A 25-year-old Private, entered military service in August, 1942, and during basic training began to complain of pain in both lower legs. In October, 1942, he was operated upon for varicose veins. He was returned to duty and felt well for several months. In December, 1942, he began to notice a recurrence of the varicose veins and discomfort in the left leg, with evidence of dermatitis in the lower leg. Because of inability to do duty, he was finally admitted to McCaw General Hospital for study and disposition. On examination, there was evidence of healed bilateral saphenous ligation scars in the groins. In the left leg there was a prominent group of varicose veins and the internal saphenous vein was palpably open up to about the midthigh. There was evidence of considerable dermatitis and discoloration of the medial aspect of the lower left leg. On Trendelenburg and Perthes' tests, the deep venous circulation was apparently competent. Venographic examination was performed (Fig. 6), and indicated that "shunting," by way of a communicating vein in the midthigh, had caused reflux from the femoral vein to the saphenous vein, thereby reestablishing the varicose veins in the lower leg. This communicating vein was readily obliterated surgically and the patient made an uneventful recovery. After an adequate period of observation, he was finally returned to full duty.

Case 4.—A 27-year-old Private, had a saphenous ligation performed for varicose veins and recurring varicose ulcer of the lower leg eight months previously. On admission to this hospital, there was a fairly large chronic ulcer on the medial aspect of the lower leg. Venography was performed and demonstrated that although the great saphenous vein had been well obliterated for most of its course, there apparently remained a markedly dilated tortuous communicating vein coming from the deep veins of the leg and establishing a "venous-lake" at the site of the chronic ulcer. This tortuous communicating vein (Fig. 4) was readily accessible for surgical ablation.

II—THROMBOPHLEBITIS, PHLEBOTHROMBOSIS, AND THROMBO-EMBOLIC ACCIDENTS

A. *Superficial Thrombophlebitis:* Superficial thrombophlebitis can be recognized clinically very readily in view of the subcutaneous location of the involved veins or previously existing varicose veins. Frequently, however, there is rapid extension of the thrombotic process to the deep venous system with meager or completely absent clinical findings to suggest such an extension. Venography of the extremities is, therefore, indicated to demonstrate the possible extension of this thrombosis, with surgical exploration of the femoral vein if there is such an extension. The venographic picture of a superficial thrombophlebitis without extension to the deep veins is similar to that of a case in which saphenous ligation has been performed (Fig. 7).

B. *Deep Vein Thrombosis:* Intravenous clotting associated with inflammatory changes in the walls of the vein usually causes the clinical picture of thrombophlebitis. That is, sudden onset of chills, stepladder rise in pulse and temperature, exquisite tenderness in the calf or along the course of the femoral vein, swelling of the limb, and signs of vasomotor disturbances. The

associated inflammatory reaction in the vein wall usually accounts for a rather firmly adherent clot, which, therefore, is less likely to become detached and cause embolization. However, it is recognized that due to stasis, a soft coagulation clot, not firmly attached to the vein wall, can, and fairly frequently does form proximal to the adherent inflammatory clot. This soft, loosely attached clot can be readily detached to form an embolic mass. Intravenous clotting, not primarily of inflammatory origin, is a condition known as phlebothrombosis. Such a clot formation is loosely attached to the vein wall and can be easily loosened with resultant embolic accident. The clinical signs of such a phlebothrombosis are entirely absent or only vaguely perceptible, and the early recognition of this extremely dangerous source of pulmonary embolization is impossible on the basis of clinical findings alone. It has been demonstrated on many occasions that venography will definitely establish an early diagnosis of deep vein clot formation. Although thrombophlebitis is commonly suspected as a complication of parturition, pelvic or abdominal surgery, it is not sufficiently realized that deep phlebothrombosis of the extremities may occur or may follow an apparently trivial injury of the lower extremity.

The importance of early recognition of deep vein thrombosis is generally recognized. It has been conclusively shown by workers in many clinics that there is a high incidence of pulmonary infarction resulting from deep phlebothrombosis with a mortality rate of eight to ten per cent in patients beyond the age of fifty. It is, therefore, obvious that the prevention of embolic accidents by femoral vein ligation is extremely important. In the younger age-group encountered in an Army General Hospital, we have performed femoral vein ligation on suspicion, or on roentgenographic demonstration, of a pulmonary infarction. In older individuals we believe it should be an established routine to perform femoral vein ligation on the basis of clear venographic demonstration of deep vein thrombosis. As previously reported by one of us, it has become regular procedure at a large municipal hospital to perform femoral vein ligation in elderly patients prior to amputation for endarteritic or diabetic gangrene. This has resulted in a sharp drop in the incidence of postamputation pulmonary complications and mortality.

Venographic pictures of deep vein thrombosis are of two distinct types, depending upon whether venography is performed during the immediate acute episode or at a later date, when organization and recanalization have occurred. It has been our opportunity to observe both types of roentgenograms. The discussion of venographic findings is concerned with deep vein thrombotic occlusion, whether of thrombophlebitic origin or essential phlebothrombosis. It is our experience with the cases which have been studied to date that we are unable to differentiate on the basis of venograms between thrombophlebitis and phlebothrombosis. The important information offered by the venogram is the detailed graphic demonstration of deep vein block.

(1) *Deep Vein Thrombosis:* The venograms of acute, immediate deep vein thrombosis are characterized by the presence of many fine "hairpin-like"

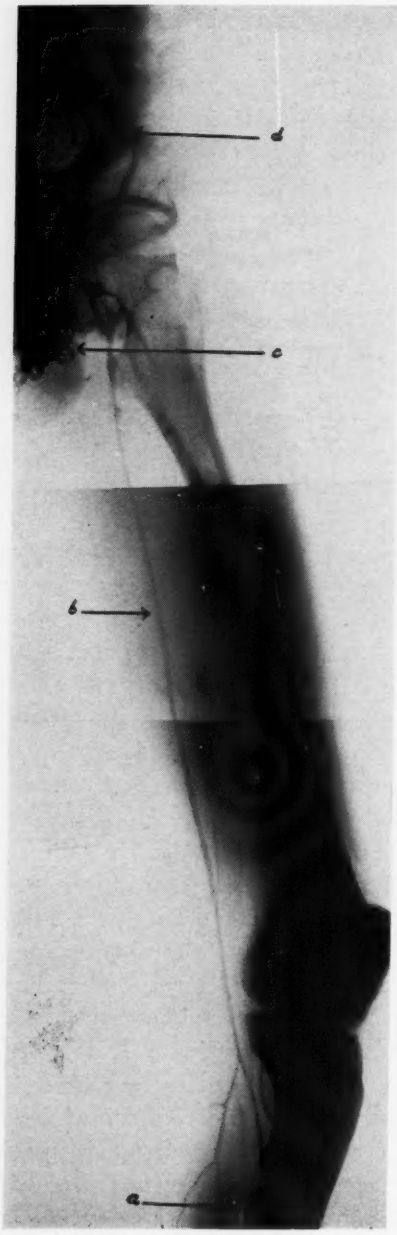

FIG. 8.—Acute Deep Vein Thrombosis of Femoral and Iliac Veins: Fine, "hairpin-like" venous markings of lower leg (a) and lower thigh. Saphenous vein filled (b) (occluded femoral and iliac veins not visualized). Overflow into superficial pudendal (c) and superficial epigastric (d) tributaries.

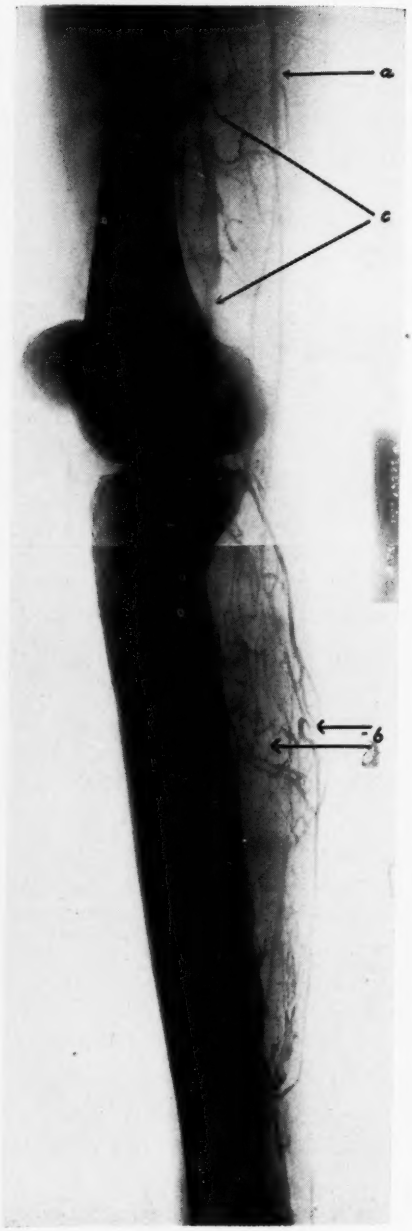

FIG. 9. — Acute Deep Femoral Vein Thrombosis: Saphenous vein visualized (a). A network of "hairpin-like" venous markings along the upper and lower leg (b), and segmental filling defects of femoral vein (c), both characteristic of *acute* occlusion.

venous markings in the leg and lower thigh (Figs. 8, 9 and 15d). These markings are probably a group of previously unused small venous collaterals. The appearance of the major deep veins from the venae comites in the leg to the femoral vein in the groin, may show sudden blunting obstruction and sharp segmental defects in the lumen (Fig. 15d). It is our impression that the venographic findings of numerous fine "hairpin-like" venous markings and sharp segmental defects are pathognomonic of acute deep vein occlusion, and that these findings have not been previously described in the literature.

Case 5.—A 23-year-old Private, was injured while on foreign combat duty, when he was struck in the right hip and thigh region with a large heavy case of ammunition. A diagnosis of a fracture of the neck of the femur was made and a large spica plaster encasement applied; the patient was then transported by airplane back to the States. On arrival at this hospital, roentgenograms of the hip were repeated and found to be negative for fracture. On the day following admission, the patient had a rise in temperature, and complained of pain in the right lower extremity. The encasement was removed and, on examination, there was suggestive tenderness in the calf region and slight edema about the lower leg and ankle. Venography was performed (Fig. 8) and demonstrated the typical findings of an acute deep vein thrombosis of the femoral vein. This patient was treated conservatively in view of the absence of any pulmonary complications, and made a satisfactory response to repeated paravertebral blocks with novocaine. This patient, after a sufficient period of observation, and convalescent furlough, has been restored to full duty.

Case 6.—A 21-year-old Private, was operated upon for a tuberculous empyema. About 24 hours after operation, the patient complained of pain in the calf of the left leg and, on examination, slight pitting edema about the ankle region and exquisite tenderness of the calf muscles was noted. Venography was performed (Fig. 9) and demonstrated all the typical findings of an acute deep vein thrombosis. In view of the extensive chest pathology already existing and the obvious difficulty in determining the occurrence of any additional pulmonary accident, it was decided to explore the femoral vein in the groin. A large fresh thrombus was evacuated from the femoral vein and the vessel was then doubly ligated and cut between ligatures. Following operation, the circulatory status of the limb returned to normal and remained so until the patient's death from miliary tuberculosis three months later.

(2) *Chronic Deep Vein Thrombosis:* We have observed and studied at McCaw General Hospital a rather large group of cases with the history and clinical findings of an old or chronic state of deep vein occlusion. These patients complained of mild to moderate swelling of the affected extremity with a feeling of weight and discomfort in the leg aggravated by prolonged standing or marching. In some cases where recanalization has been fairly ample, symptoms and findings in the lower extremity may be very mild. The venographic picture in the case of chronic or old deep vein thrombosis is characterized by a partial or total absence of visualization of the femoral vein, the popliteal vein or the venae comites of the leg. Marked irregular narrowing defects or the so-called "patchy or moth-eaten appearance" of the vein may be noted (Fig. 15e). The latter has been described as "mantle filling" by other authors. In some instances, tortuous collateral vessels may be seen to "bridge over" a defect in the main vessel (Fig. 10). The superficial venous return is usually quite prominent and may be responsible

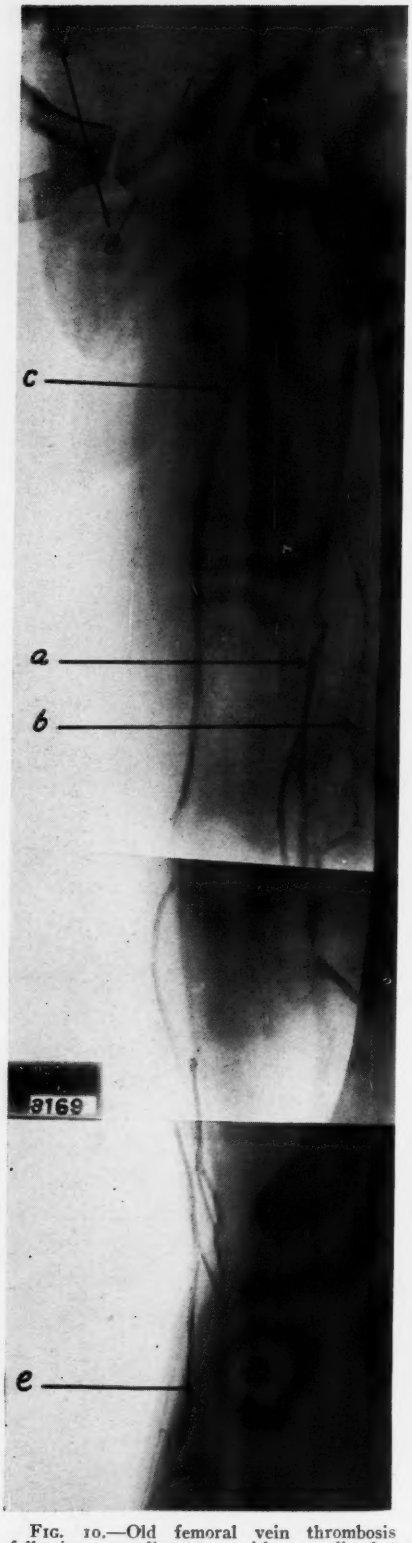

FIG. 10.—Old femoral vein thrombosis following appendicectomy, with recanalization (a) and bridging (b) of the involved portion. Note prominence of great saphenous vein (c) and overflow into external superficial pudendal vein (d). Varicosities of both internal and external saphenous vein in the lower leg (e).

FIG. 11.—Old femoral vein thrombosis following appendicectomy and gas bacillus infection, aggravated by saphenous ligation and sclerosing therapy of varicosities seven years after appendicectomy. Present clinical picture of severe lymphedema of the leg. Patchy moth-eaten femoral vein (a). Great saphenous vein not visible (recent ligation). Bridging of femoral defect (b).

for the formation of varicose veins. In many cases of deep vein occlusion, the superficial venous tributaries in the groin and lower pelvis (the superficial external pudendal, the superficial iliac circumflex and the superficial epigastric) are visualized as extremely tortuous and prominent. These tributaries have never been vizualized in the venograms of the normal extremity, and are considered to be characteristic of old, deep femoral vein occlusion. These tortuous veins in the groin may become so prominent as to cause an erroneous diagnosis of femoral hernia, as will be described in one of the case reports. Again, we wish to emphasize that the venographic findings of numerous fine, wavy, hairpin-like venous markings are not encountered in the old or chronic cases in which recanalization and compensatory venous return of the extremity has been established, but only in the cases of acute or immediate deep vein thrombosis.

It is interesting that in about 50 per cent of the cases of old or chronic femoral vein occlusion observed at this hospital, the acute episode had occurred about ten days following appendectomy.

Case 7.—A 32-year-old Private, was operated upon for acute appendicitis nine months previously. On the ninth day of an apparently uneventful postoperative course, he developed the rather typical findings of an acute deep vein thrombosis. Because of obesity and persistent symptoms of swelling and discomfort in the leg on walking, the soldier was admitted to this hospital for study and disposition. Venography (Fig. 10) demonstrated definite evidence of an old, deep vein thrombosis, partially recanalized, with compensatory varicose veins. This patient was recommended for separation from the service.

Case 8.—An obese 38-year-old Private, was operated upon for acute appendicitis in 1934. He developed a gas gangrene infection of the abdominal wall, requiring multiple extensive incisions of the lower abdomen and thigh region. Shortly thereafter he was aware of considerable discomfort and tenderness in the right calf followed by a moderate degree of swelling of the right lower extremity. Subsequently, he began to notice the presence of prominent varicose veins in the right lower extremity, with little or no symptoms referable to the presence of these veins. In November, 1942, shortly after induction into military service, this soldier was treated with saphenous ligation and several injections of sclerosing solution into the varicose veins. Shortly thereafter, he developed a severe, painful swelling of the entire right lower extremity, with marked acute inflammatory signs. This condition subsided after several weeks of bed rest and wet dressings. He was admitted to this hospital, in August, 1943, for study and disposition; venography (Fig. 11) was performed and demonstrated the existence of an old, deep vein thrombosis. It is our impression that this condition had occurred during or shortly after the series of surgical procedures in 1934; and that the superficial varicosities were a part of the compensatory mechanism for venous return. The performance of saphenous ligation, followed by the use of sclerosing injections, without information concerning deep vein pathology, apparently brought on a severe inflammatory reactivation of the old thrombotic process, with further embarrassment of the return venous circulation. This soldier was eventually recommended for separation from the service.

In other cases the acute deep vein occlusion has apparently occurred insidiously or following relatively mild trauma to the extremity. In this latter group the presence of a deep phlebothrombosis had been overlooked in some instances.

FIG. 12.—Old femoral vein thrombosis following severe ankle sprain. Subsequent development of tortuous venous tributaries in the groin, led to erroneous diagnosis and surgical exploration for femoral hernia. Patchy moth-eaten appearance of femoral vein (a). Prominent great saphenous vein (b). Overflow into superficial external pudendal vein (c) and circumflex iliac vein (d). Compensatory varicosities of lower leg (e).

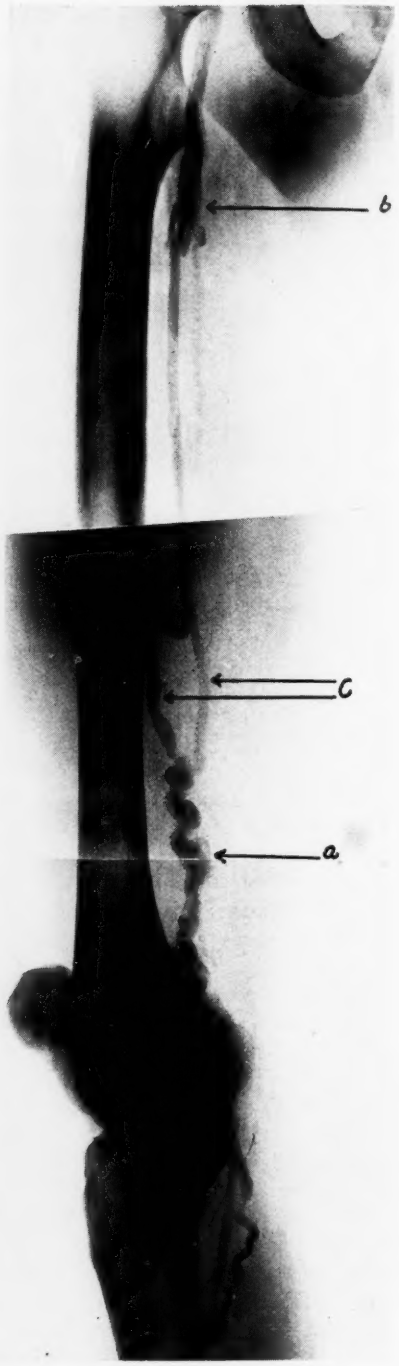

FIG. 13.—Rare Observation of Tortuous Dilatation of Lower Femoral Vein (a): Old deep vein thrombosis (b). Bridging of femoral vein (c). Great saphenous vein not visualized (surgical ligation). Chronic leg ulcer following saphenous ligation in the presence of undiagnosed deep vein pathology.

Case 9.—A 40-year-old 1st Lieutenant, suffered a sprain of the ankle and lower leg in February, 1943, while on foreign duty. This was treated with several days of bed rest, elevation and application of wet dressings. About one week later there was a recurrence of pain in the lower leg, with pain, swelling and tenderness in the thigh and groin. This discomfort and swelling of the lower extremity subsided to a moderate degree. Four months later, because of a persistent bulge in the groin, the patient was operated upon for femoral hernia. The operative report states that no hernia was found but that a group of enlarged tortuous veins was encountered in the region of the fossa ovalis. The officer was referred to this hospital for study and disposition. The physical findings in the lower extremity were those of mild pitting edema and presence of a moderate number of superficial varicose veins in the leg. Venographic examination (Fig. 12) demonstrated an old venous thrombosis with recanalization and marked tortuous dilatation of the superficial pudendal, epigastric and circumflex iliac veins in the groin and lower pelvis. History and findings indicated that the presence of a deep vein thrombosis following ankle sprain had been overlooked, and the prominent venous bulge of tributaries in the groin had been erroneously diagnosed as a femoral hernia.

In some cases the original clinical history was that of pneumonia, with three to four recurrences of acute pulmonary episodes characterized by severe chest pain, bloody sputum, chills, spiking temperature and roentgenologic evidence of pulmonary pathology. Obviously, these were manifestations of recurring pulmonary embolic accidents originating in a deep thrombosis of the lower extremity. Were such accidents to occur in an older age-group of patients, a definite mortality rate would be encountered. Venography in such suspicious or suggestive pulmonary conditions would reveal the source of emboli, with proper performance of femoral vein ligation.

Case 10.—A 26-year-old Corporal, suffered an acute chest condition in December, 1942, which was diagnosed as pneumonia. At about the same time he noticed pain and swelling of the left leg, which he believed had followed a trivial injury to his leg shortly before entering the hospital. He was making a satisfactory recovery until two weeks later, when he again developed pain in the chest, a sharp rise in temperature and blood-streaked expectoration. Patient was hospitalized for an additional month and then discharged to duty. Because of continued swelling and discomfort in the left lower extremity, he was referred to McCaw General Hospital for further study. On examination, there was slight pitting edema of the lower two thirds of the leg and some evidence of vasomotor disturbance. Venography revealed definite evidence of an old, deep vein thrombosis involving the popliteal and femoral veins. It is our impression that the presence of an acute deep vein thrombosis was the source for the original embolic pulmonary infarct diagnosed as pneumonia.

Case 11.—Another extremely interesting case of combined pulmonary and deep vein pathology was observed. A 28-year-old soldier, was admitted for study three months after his first attack of "pneumonia." He subsequently had three additional episodes of so-called relapsing pneumonia at intervals of two to three weeks. Roentgenologic studies of the chest suggested the possibility of recurring infarctions, and venography demonstrated the presence of an old, deep vein thrombosis. Because of these recurring episodes, it was felt that complete organization of the thrombotic process had not occurred, even at this late date, and that embolic masses were breaking off periodically. Femoral vein exploration and ligation was performed, with demonstration of an old thrombotic process. This patient was subsequently sent on furlough, and then returned to the hospital for an adequate period of continued observation. The patient remained entirely well, and has since been returned to full duty.

Case 12.—A 38-year-old Private, was referred to McCaw General Hospital because of recurring ulceration of the medial aspect of the left lower leg. About 15 months ago, shortly after entering military service, he had a saphenous ligation, with retrograde sclerosing injection, for varicose veins of the lower leg. The patient stated that prior to ligation, he had had considerable discomfort and aching in the left leg induced particularly by drilling and marching; however, he had had no inflammation or ulceration of the skin. Shortly after ligation, this soldier developed a rather large ulceration on the medial aspect of the left lower leg. When treated with absolute bed rest and elevation of the leg, the ulcer healed. However, on each occasion when the soldier was sent back to duty, the ulcer promptly recurred, requiring almost continuous hospitalization. Venography was performed (Fig. 13) at this hospital and revealed evidence of an old thrombosis of the upper femoral vein, with marked tortuosity and dilatation of the lower femoral vein (this type of tortuosity of femoral vein has never been visualized before in any of our venographic studies). It is our impression that this soldier had had a previously unrecognized deep vein pathology, with secondary superficial varicose veins; and that, here again, saphenous ligation for varicose veins in the presence of impaired deep vein circulation had aggravated the pathology and resulted in a chronic leg ulcer. This soldier was considered unfit for active duty and recommended for separation from the service.

FIG. 14.—Visualization of Iliac Vein (a).

A survey of these cases of old or chronic deep vein thrombosis reveals that the residual sequelae of mild to moderate lymphedema of the extremity with associated discomfort on prolonged standing or walking and some vasomotor symptoms, are more or less permanent. Although various measures can be utilized to control or minimize the discomfort of these symptoms, the fact remains that once lymphedema of an extremity has been in existence for a period of months, there is no curative therapy available except for radical surgery in a very low percentage of cases which go on to elephantiasis proportions. Therefore, the majority of the cases which we have seen late in the existence of pathology required separation from the service because of swelling and discomfort in the extremities. On the other hand, were these cases to be recognized immediately after the occurrence of the acute deep vein thrombosis, we believe that the utilization of repeated paravertebral block, in the inflammatory thromboplebitis cases, and heparin or dicoumerin therapy, would prevent delayed residual symptoms due to swelling of the limb; and that prompt femoral vein ligation, when indicated, would prevent the danger of an immediate embolic accident. It is not our particular purpose in this communication to elaborate on the etiology or therapy of deep phlebothrombosis and thrombophlebitis, but essentially to stress the fact that immediate diagnosis

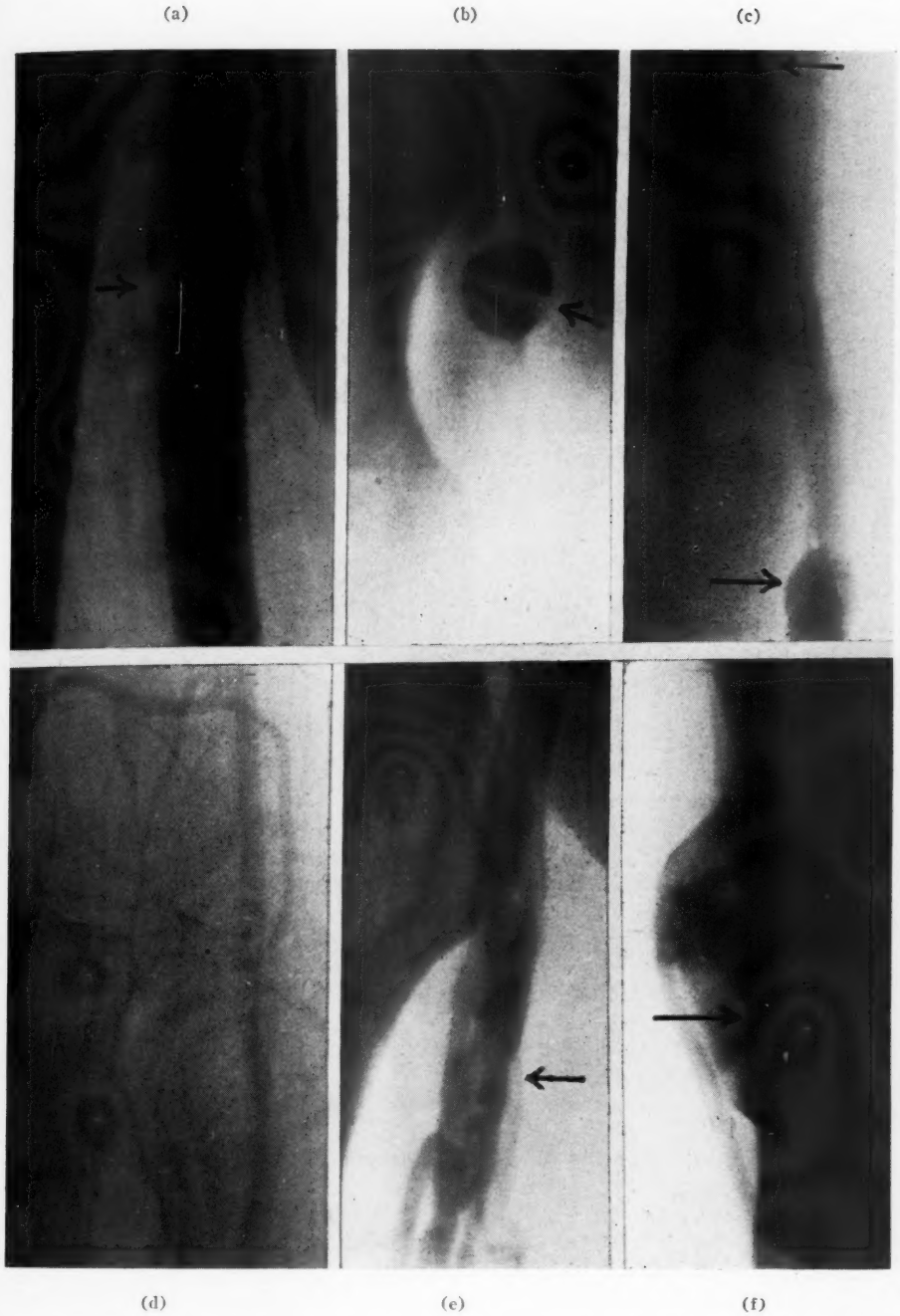

FIG. 15.—Normal valve, profile view (a). Normal valve, axial view (b). Paravalvular bulging (c). "Hairpin-like" venous markings and segmental defects of acute deep vein thrombosis (d). Patchy moth-eaten femoral vein in chronic deep vein thrombosis (e). Cauliflower varicosity (f).

of an acute thrombotic process of the deep veins is important, and can be best demonstrated by the use of venography.

SUMMARY

1. The roentgenologic technic and various diagnostic criteria of pathology in the venous circulation of the lower extremities have been described and illustrated.

2. The clinical case-groups of venous disturbances of the lower extremities encountered at an Army General Hospital have been described in relationship to their study by venography.

3. The importance of venography in the study of (a) recurrent varicose veins and their complications; and (b) thrombosis of the veins of the lower extremities, is illustrated in a group of case reports.

4. Particular stress is placed upon the immediate diagnosis by venography of the acute thrombo-embolic processes in the lower extremities with respect to prompt femoral vein ligation in the prevention of pulmonary embolic accidents.

5. It is our belief that many of the late disabling sequelae of deep vein thrombosis of the lower extremities could be prevented by prompt recognition with venography and the prompt use of the recognized therapeutic measures.

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PECTUS EXCAVATUM

REPORT OF TWO CASES SUCCESSFULLY OPERATED UPON

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UNTIL Dr. A. Lincoln Brown[1] reported his operation, experiences with the correction of the deformity known as pectus excavatum were disappointing. The application of traction by various methods and the several plastic procedures, mostly of a minor and inadequate nature, were of necessity doomed to failure when considered in the light of an accurate understanding of the anatomic facts regarding the deformity. There were obvious objections to resection of a part of the sternum, although that radical procedure was of course better calculated than any others then available to relieve extreme degrees of pressure upon, or displacement of, the heart.

At the Massachusetts General Hospital our attempts to correct or relieve the condition in a few cases resulted in complete or partial failure, and the thought of operating upon such patients had been practically abandoned.

In 1943, the opportunity arose to apply the principles put forth by Doctor Brown. The success of the operation in these two cases prompts me to report them in considerable detail. It is desirable also to propose certain minor modifications of technic which may be worth the consideration of those who have occasion to perform this ingenious operation.

In May, 1943, Dr. Paul White referred to the Surgical Service two sisters, age 14 and 5 years, respectively, for consideration of the possibility of surgical correction of pectus excavatum. The elder child had suffered serious circulatory disturbances as a result of this deformity, which in her case was of extreme degree. But in addition she was much disturbed emotionally because of the anomaly. Her embarrassment because of the deformity was so extreme that she refused to wear a bathing suit, and was exceedingly shy about allowing anyone but her physicians to see her chest without clothing. She had grown rapidly and was taller than other girls of her age. She was so sensitive about her unusual height that she had accentuated her naturally stoop-shouldered posture so as to diminish her apparent tallness. The resulting poor posture tended to accentuate the chest wall deformity. Thus, she presented two cardinal indications for surgical correction of the pectus excavatum, namely, disturbances of the circulatory mechanism and the unfavorable effect of the deformity upon the psychology of the patient. In the hope that her appearance might be improved, this child was eager to be operated upon.

In the case of the younger sister no symptoms had been observed and she was too young to be disturbed about her appearance. But the deformity had become steadily more prominent as she had grown from infancy.

There was no clear-cut history of other examples of the deformity in the family. There were four siblings, all of whom were normal. The father, who was normal, had died. Their mother was of the impression that one paternal uncle had a pectus excavatum, but her knowledge of her husband's family was incomplete. The mother's family was free from any suggestion of the deformity for at least several generations.

ANATOMIC CHARACTERISTICS OF THE DEFORMITY

Without attempting to elaborate upon the possible causes of pectus excavatum or to improve upon the excellent description of the abnormal anatomy given by Brown,[1] several impressions resulting from the study of the two sisters referred to in this communication are presented. In each case the diaphragmatic attachments to the sternum, the importance of which is stressed by Brown, were found and cut as a part of the operative technic, but these structures were not abnormally large or strong. The substernal membrane or ligament did not appear to be a very important structure in these cases. The degree of depression of the gladiolus, however, was so severe in the older girl that the apex of the funnel-shaped deformity was actually about 1 cm. posterior to the plane of the anterior surface of the vertebral bodies and to the left of them. In the younger girl there was just room enough during expiration to insert a finger between the deepest portion of the sternum and the anterior surface of the vertebral bodies.

The skeletal deformity in both cases was characterized by what appears to be an anomaly of both the sternum and the costal cartilages, and of necessity the costochondro-sternal articulations of the lower three or four ribs. One is impressed in pectus excavatum by the fact that the gladiolus of the sternum, after being freed from its attachments within the mediastinum and liberated from the costal cartilages so as to bring it up from the bottom of the deep depression, is of essentially normal size and shape. Its upper portion near the manubrio-gladiolar junction has a posterior inclination, but once this has been corrected by a wedge-shaped transverse osteotomy the gladiolus appears to be normal. Its inferior end, actually at its junction with the xiphoid, represents the deepest point of the funnel deformity, the sides of which are made up of costal cartilages, upper abdominal wall, xiphoid, and gladiolus itself. When the deformity is well marked, no amount of release of pull by dividing the substernal attachments of the diaphragm, the ligaments, or the fasciae would appear to have much effect on improving the condition. In the cases with a deep depression it seems almost as though the sternum is pushed down against the spine by unusually long, inward-curving costal cartilages rather than that it is pulled down to the spine by the attachments beneath. Experience with the operation proposed originally by Brown, and described here, demonstrates that unless appreciable lengths of the lower costal cartilages are resected, it is impossible to correct the deformity even after releasing the pull of the substernal diaphragmatic and fascial attachments and the removal of a wedge of bone at the upper limits

of the gladiolus. One gets the impression, therefore, that the deformity may be primarily skeletal.

That there is, however, an inward motion of the lower end of the sternum during inspiration was well demonstrated in each of the two girls whose cases are under discussion. This was obvious from the measured decrease in the anteroposterior diameter of the chest on deep inspiration as compared with full expiration. It was also observed at operation most strikingly in

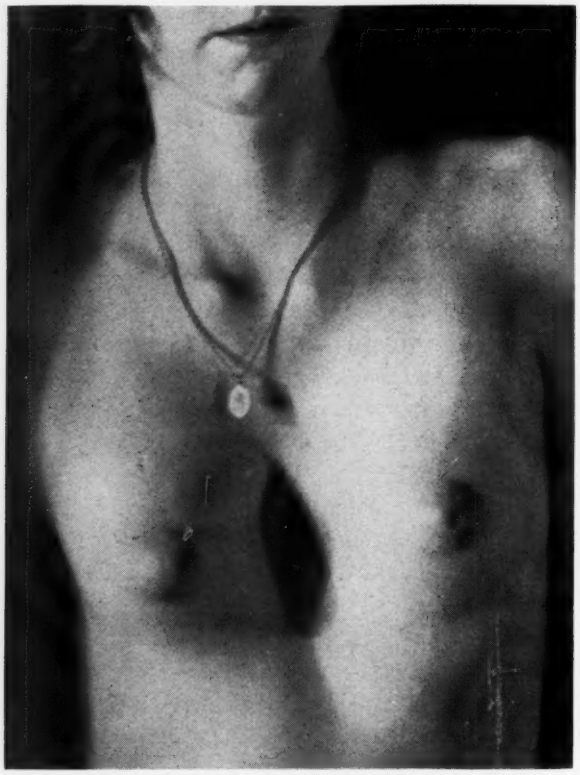

FIG. 1.—Case 1: Preoperative appearance of the chest, showing marked pectus excavatum. Note the locket hanging off the chest wall because of the funnel-shaped depression.

the younger child. In her case at operation during expiration there was just room enough to insert the index finger between the posterior surface of the sternum and the anterior surface of the spine. But during inspiration the sternum was depressed so firmly that the finger could not be withdrawn until released by the relaxation which occurred during expiration. This occurred even after the diaphragmatic attachments to the sternum itself had been severed.

CASE REPORTS

Case 1.—M. G. H. No. 343479: J. H., female, age 14, was admitted to the Massachusetts General Hospital, September 7, 1943, because of a marked funnel chest deformity,

which had been present since birth and which had become worse as the patient had grown older. About four years before admission she had begun to have attacks of palpitation coming on at irregular intervals and lasting from four to 24 hours. During these attacks the pulse had been regular, but the rate had gone up as high as 150 according to the patient's mother. She had had no dyspnea, chest pain, or pain in the arms associated with these attacks, but her mother said her lips had been blue during them. Following the attacks she had occasionally had slight pain in her chest lasting for an hour or two. There had never been any evidence of rheumatic fever or joint trouble.

FIG. 2.—Case 1: Plaster model made directly from the patient by Dr. Carroll Larsen for the purpose of studying the deformity and as a permanent record for future comparison. This shows the extreme depth of the sternal depression somewhat more clearly than the photograph of the patient.

She had been studied in the Cardiac Clinic where a diagnosis of paroxysmal tachycardia had been made. On roentgenologic examination it was found that the lower extremity of the sternum touched the vertebral bodies. In the anteroposterior view the heart shadow was entirely in the left hemothorax extending to the left chest wall. The transverse diameter of the heart was 14.5 cm. The internal diameter of the thorax was 23.5 cm. In the right anterior oblique view the transverse diameter of the heart became 11.2 cm. and in the lateral view the depth of the heart measured about 8.4 cm. The heart appeared to be enlarged as well as flattened. An electrocardiogram showed rather marked right axis deviation with slight elevation of ST_1 and slight depression of ST_3, which was interpreted as evidence of quite marked right

ventricular strain and hypertrophy. These changes were believed to be dependent upon compression of the heart by the sternal deformity rather than on an associated cardiac defect, congenital or valvular. A consultation was, therefore, requested as to the possibility of surgical correction of the deformity.

There was no definite family history of funnel chest, but the patient's sister, five years old, had the same condition. Her father was known to have heart disease for a few months prior to his death from coronary thrombosis a year before her admission to the hospital and a paternal uncle and grandfather had some heart disease.

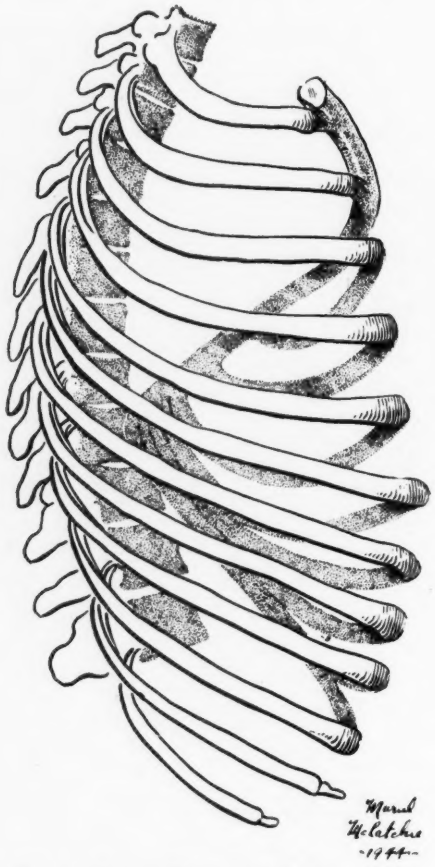

FIG. 3.—Case 1: Diagram of rib cage. Lateral view showing the relation of the sternal depression to the dorsal spine. Note the elongation and deep incurving of the lower costal cartilages.

Physical Examination.—This showed a tall, thin girl, age 14, with a long thin chest. There was some left middorsal scoliosis with a reverse dorsal curvature of the spine above this, but no kyphosis. There was marked depression of the sternum with a distance of only 9 cm. between the front of the sternum at the depth of the deformity and the back of the spine. The trachea was deviated to the left and the entire heart appeared to be pushed into the left chest. The pulse was regular at 80. Blood pressure 130/80. There was no edema and no evidence of arthritis. The lungs were clear and resonant. On examination of the heart the apex impulse was felt in the seventh interspace in the midaxillary line, 12 cm. from the midsternal line and 4 cm. beyond the midclavicular line. There was no dullness above the third rib, but the left border of cardiac dullness

agreed with the palpable impulse. The right border extended to the sternum. P2 was double. There was a moderate harsh systolic murmur at the apex, slight at the base. No diastolic murmurs were heard. The apical systolic murmur was loud at the left lung base in the back. Chest expansion at the upper thoracic level was 1 inch, at the lower thoracic level 1.5 inches, measured with the spine straight.

Laboratory examination of the urine was negative. The red blood cell count was 5,700,000, and the hemoglobin 90 per cent. Hinton test was negative.

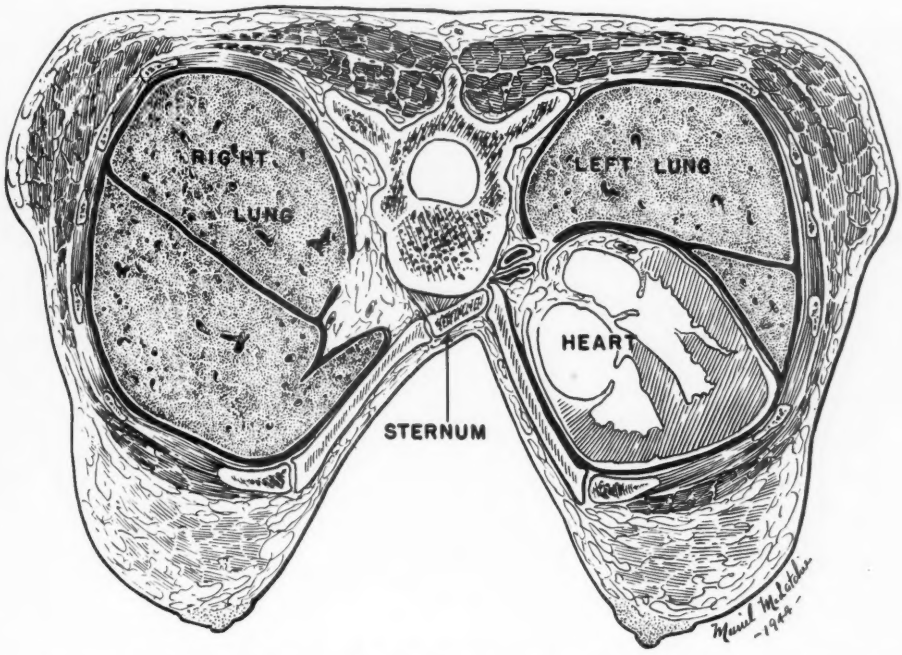

FIG. 4.—Case 1: Diagram showing the relations of the viscera and the chest wall deformity at the level of the apex of the funnel-shaped depression just above the junction of the xiphoid process with the gladiolus. Note the heart pushed completely into the left side of the chest with its apex against the left lateral wall of the thorax. The deepest point of the depression is actually posterior to the plane of the anterior surface of the vertebral bodies.

Operation was planned for October 1, but after the patient had reached the operating room, she had a sudden attack of paroxysmal tachycardia, with cyanosis and slight congestion of the neck veins. The pulse rate was over 160, and the blood pressure fell to 80 mg. of Hg. systolic. There was prompt relief after the intravenous injection of 6 cc. of cedilanid and on October 3, the patient was started on two grains of quinidine t. i. d. Her course was satisfactory and operation was finally performed on October 9, 1943.

Operation.—A vertical midline incision was made. The xiphoid process was removed, the rectus abdominis muscles were reflected from their attachments to the sternum and adjacent costal cartilages, and the diaphragmatic attachments were cut. The costal cartilages were then divided, but it was observed before this was done that the sternum was pulled in so deeply that it lay to the left and posterior to the anterior surface of the vertebral column. After cutting the costal cartilages all the way up to the second, it being necessary to divide the third in this patient, a transverse wedge-shaped piece of bone was removed from the sternum just below the articulations of the second cartilages. Three wire sutures were used to hold the trimmed lower portion of the sternum up in the proper position. Large segments of costal cartilage were

removed, fitting each one in turn so as to restore the chest to a reasonably normal contour. These were held in place by heavy silk sutures. Following this the muscle layers were reattached excepting the diaphragm. In closing the skin it was necessary to remove a redundant portion from one side because of the fact that after the deep funnel-shaped deformity had been corrected, there was too much skin.

The patient's postoperative course was complicated only by two attacks of paroxysmal tachycardia occurring one day and 12 days after operation, with improvement on administration of quinidine. An electrocardiogram taken on the 12th day showed the P waves more prominent than formerly. She was instructed in good posture and arm positions to assist in chest elevation and was discharged in good condition on the 17th postoperative day.

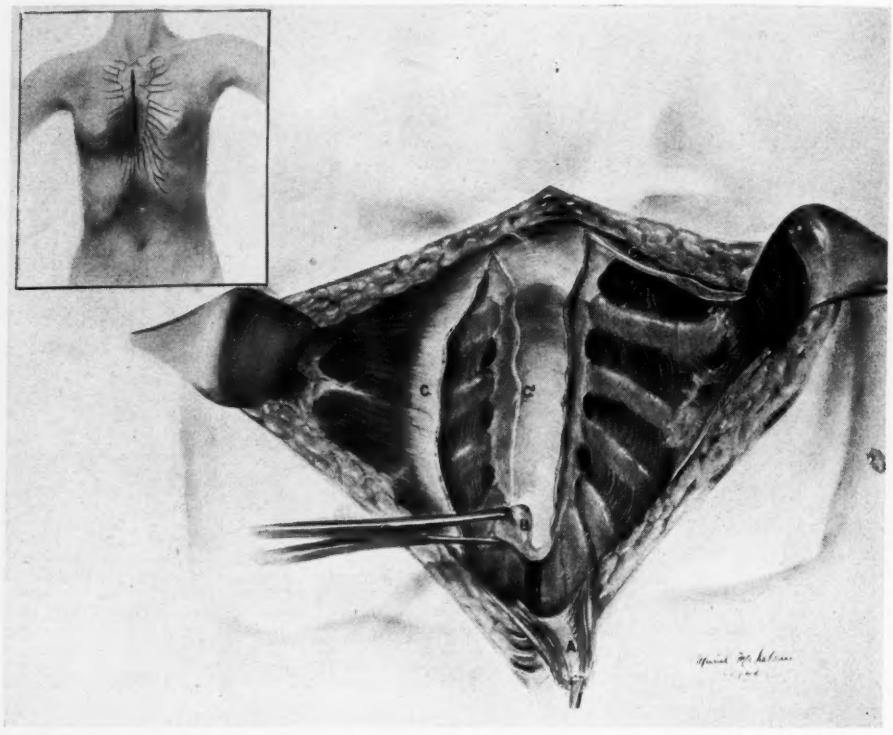

FIG. 5.—Case 1: Beginning of operation showing exposure. Insert gives line of incision. (A) Linea alba and a portion of each rectus abdominis muscle reflected after freeing from xiphoid and lower costal margin; (B) xiphoid process held up with tenaculum; (C) fascia of the pectoralis major muscle after separating it from the anterior surface of the sternum (C'); (D) pectoralis major muscle freed from underlying costal cartilages and retracted.

The patient reported for a postoperative check-up a month after discharge from the hospital. She had been fairly well except for a few short spells of paroxysmal tachycardia. The wound was well healed. The sternal depression was largely corrected so that the distance from the front of the sternum to the back of the spine was about 13 cm. The apex impulse was felt in the fifth interspace, 9 cm. to the left of the midsternal line. The systolic murmur was present in the left back as before. Fluoroscopy showed a large heart shadow, rather flattened anteroposteriorly and largely in the left thorax, but there was much more room in the mediastinal space. An electrocardiogram showed little change. T2 was less inverted, which was interpreted as possibly a sign of decreased right ventricular strain.

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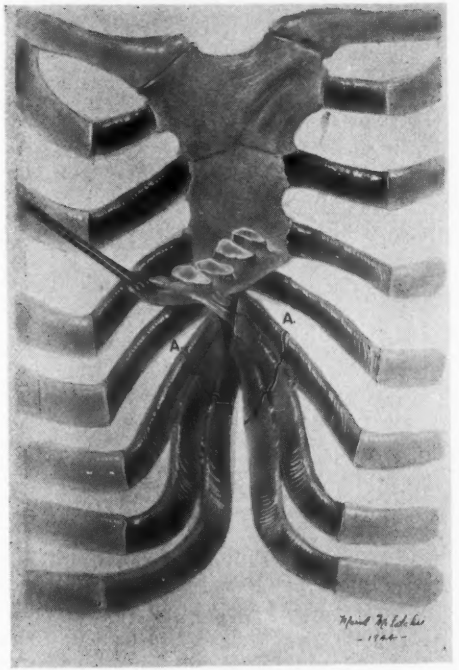

FIG. 6.—Case 1: Diagram to illustrate freeing of the sternum from the costal cartilages. The third cartilages have not yet been cut across. Note how the cartilages fall together after pulling sternum up. Line A indicates the location of the final divisions across the cartilages. All the cartilage between this line and the margin of the sternum is to be discarded.

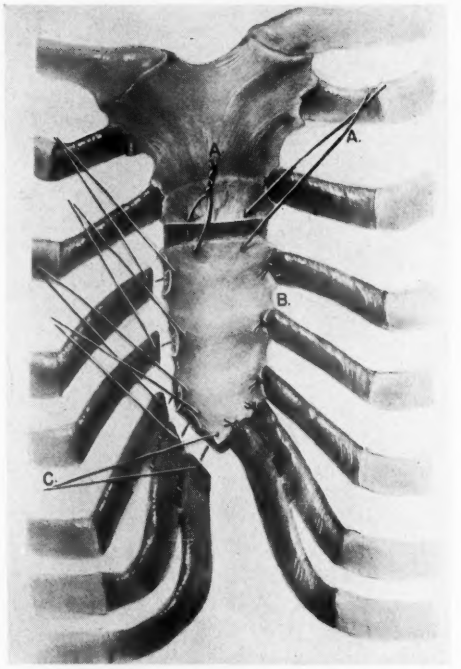

FIG. 7.—Case 1: Diagram to illustrate the method of fixing the sternum in its elevated position by wire sutures, (A) which approximate the edges of the defect left after removing a transverse wedge of the bone below the level of the second costal cartilages. Heavy silk sutures used to fasten the costal cartilages to the sternal edge shown tied on the left (B) and ready to be tied on the right (C).

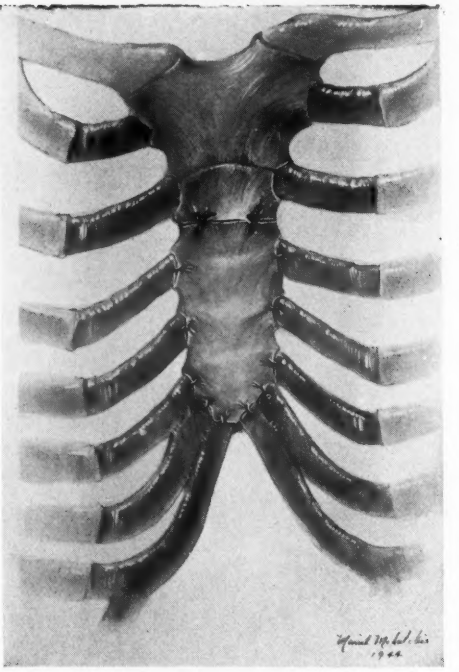

FIG. 8.—Case 1: Diagram showing all sutures in place after trimming the cartilages and removing a transverse wedge from the sternum, thus correcting the funnel-shaped depression.

Case 2.—M. G. H. No. 384900: P. H., female, age 5, sister of the patient described in Case 1, was admitted to the Massachusetts General Hospital, September 9, 1943, because of an apparently congenital funnel chest deformity. When the patient was six months old the mother had first noticed a depression of the anterior chest which had become more prominent as the patient became older. She had had no complaints and her activity had not been limited. There was no history of bone pain, fractures, swelling or pain in the joints. She had been seen in the Cardiac Clinic ten months prior to admission, where a diagnosis of funnel chest, with displacement of the heart

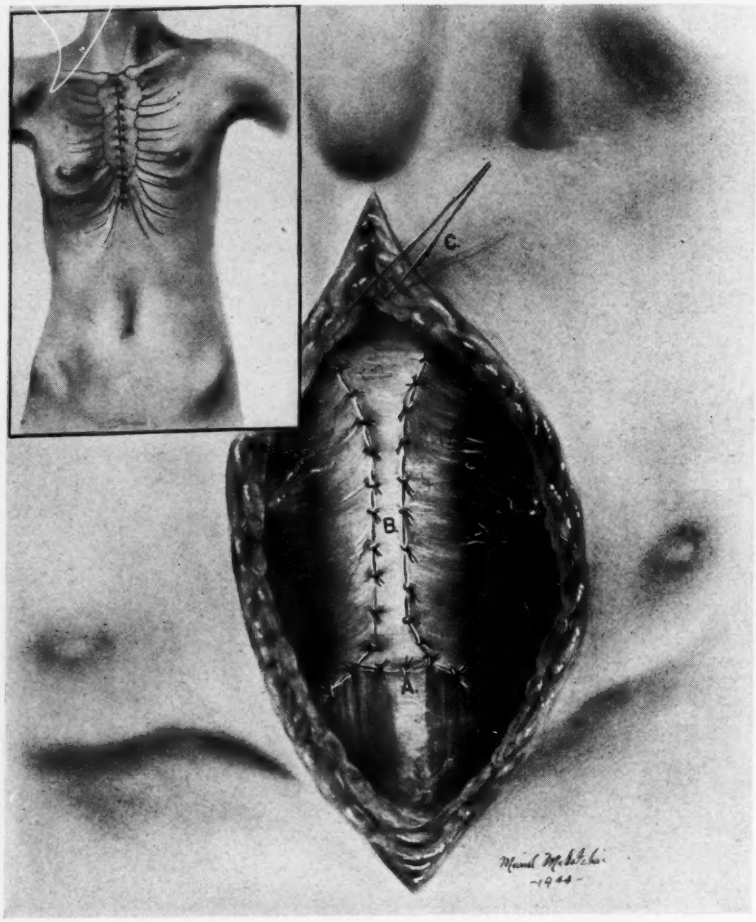

FIG. 9.—Case 1: Completion of the operation. Diagram showing suture of rectus muscles and linea alba to the lower costal cartilages and sternum (A); suture of pectoralis major muscle fascia to the sternum on each side (B); closure of the superficial fascia and fat begun (C). Insert shows completion of skin closure.

to the left and questionable cardiac compression had been made. Examination of the heart at that time by fluoroscope showed it to be almost entirely in the left chest and not much enlarged. An electrocardiogram was reported to be within normal limits.

Physical Examination.—This showed a well-developed and well-nourished girl, with good color. There was a large, hemispherical depression in the mid and lower sternum, about 3 x 3 cm., with characteristic sinking-in on deep inspiration. There was a moderate degree of scoliosis, apparently structural, with convexity to the left in the thorax and to the right in the lumbar region. Examination of the heart showed

the apex in the midaxillary line, impulse forceful, sounds of good quality. Rate was 100 and rhythm regular, with a rare extrasystole. There was a double mitral murmur of moderate intensity as well as a Grade III late apical systolic murmur heard all over the precordium, which became louder as one went to the left around the chest, becoming maximum, Grade IV, posteriorly just under the angle of the scapula on the left. There was a palpable thrill transmitted to the left axilla and pulmonic region. There was no diastolic murmur. The heart was apparently in the left chest, with the point of maximum impulse 4 cm. to the left of the midclavicular line. Vital capacity 870.66 cc. Blood pressure 90/65.

FIG. 10.—Case 1: View of chest two and one-half months after operation, showing correction of deformity.

Roentgenologic examination of the heart showed it displaced entirely into the left chest by the thoracic deformity, the apex reaching almost to the left lateral chest wall. It did not appear to be enlarged. An electrocardiogram revealed the axis shifted to the right with the P waves inverted and diphasic.

Examination of the urine showed it to be normal. The red blood cell count was 4.46; white cell count 9,600. The nonprotein nitrogen was 12 mg., and the serum protein 6.8 per cent.

Operation.—September 25, 1943: A vertical incision was made in the midline from the manubrium of the sternum to the upper abdominal wall. This was deepened down to the sternum. The xiphoid process was then freed-up and the attachments of the rectus muscle were freed from the costal margin and retracted. The sternal attachments

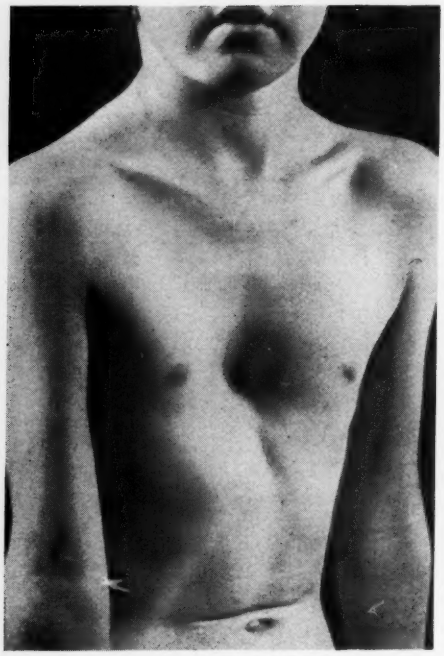

FIG. 11.—Case 2: Preoperative appearance of chest showing characteristic depression of lower portion of sternum.

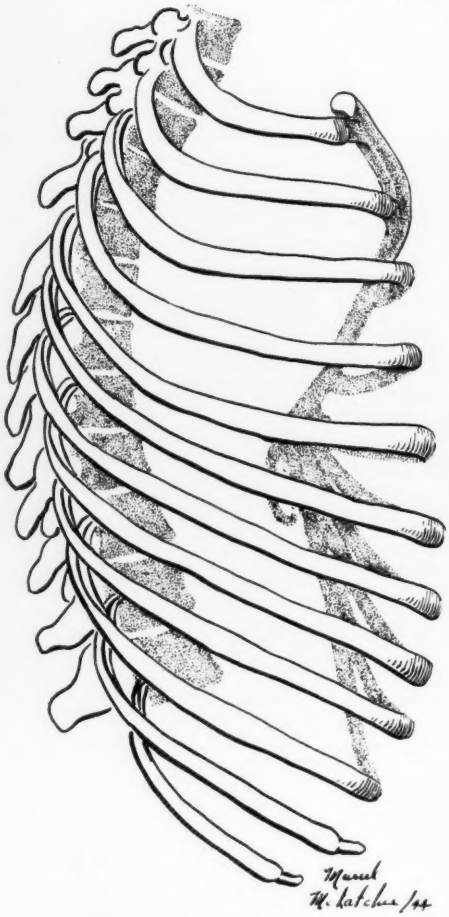

FIG. 12.—Case 2: Diagram of rib cage showing depth of sternal depression in this case.

of the pectoralis muscles were then severed and retracted. The costal cartilages, beginning from below and working upwards, were then cut across about 1 cm. from the sternum and division was carried up to the third cartilage on each side. The sternum was trimmed so as to free it of any costochondral attachments. A transverse osteotomy was performed with the rotary saw across the sternum just below the articulations of the third costal cartilages and a wedge-shaped piece of bone removed. The lower portion of the sternum was swung up and, using two wire sutures to close the gap where the wedge had been removed the lower portion of the sternum was held in a new position, thus correcting the funnel deformity. Segments of cartilage were removed on each side so as to make the rib cartilages fit the sternum again and these cartilages were held to the sternum in its new location by means of heavy silk sutures.

Except for a urinary tract infection the patient's postoperative course was uneventful. Roentgenologic examination of the chest showed the heart still placed somewhat to the left. She was started on postural exercises before leaving the hospital and was to be followed in the Posture Clinic.

She was seen for a follow-up visit on November 19, 1943. The functional and anatomic results were excellent. She was gaining weight, her color was good, and she looked better than before operation. She was cooperating very well with her exercises, and gave a good demonstration of her deep breathing and postural correction. The scar was smoothly healed. An electrocardiogram, November 24, showed little change from the preoperative tracing except with respect to the P waves (at first

diphasic to inverted in leads 1 and 2), with slight axis deviation in all records. Fluoroscopy showed the heart still somewhat displaced into the left chest, but there was ample mediastinal space.

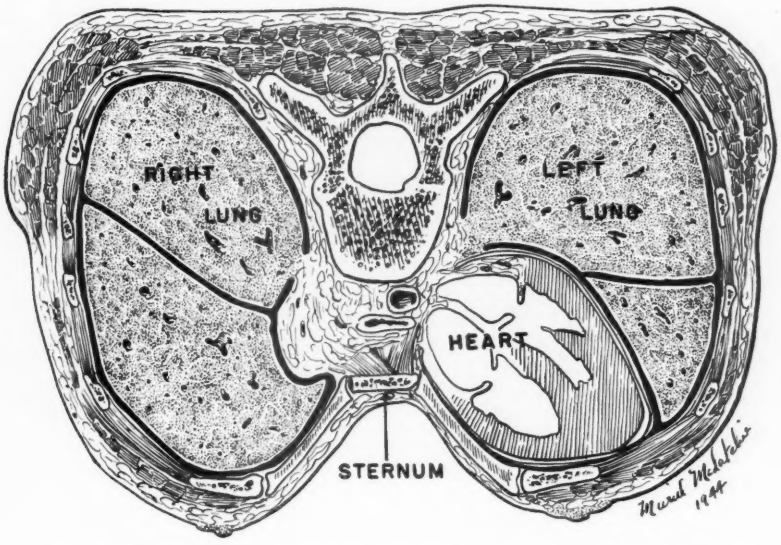

FIG. 13.—Case 2: Diagram showing relations of the viscera and the chest wall deformity at the apex of the funnel-shaped depression. Note the heart pushed to the left but not so far as in Case 1.

TECHNICAL CONSIDERATIONS

In general, the principles suggested by Doctor Brown were followed in the treatment of these two patients. The following minor departures from his method should be mentioned:

(1) A straight midline incision was used instead of the curved semicircular incision. This would seem to be preferable because it gives an exposure which is equally good on both sides of the sternum with a minimum of interference with the circulation to the skin edges.

(2) Excepting for the closure of the transverse osteotomy defect, heavy silk (No. 4 Deknatel) was used instead of wire to approximate the trimmed costal cartilages to the edges of the sternum. The silk gives adequate tensile strength and is more pliable.

(3) No external traction apparatus was employed to keep the sternum in place. Experience with these two cases demonstrates that this part of the procedure is not necessary.

(4) A light breast plate of plaster was made at the end of the operation in each case and moulded so as to fit the contour of the anterior chest wall over the gauze dressing. This was used to help stabilize the anterior chest wall during the first week after operation, during the time when there is such a great tendency to paradoxical motion of the chest wall during respiration. A plaster plaque such as was used in these cases has been found to be an invaluable assistance in the early convalescent-period after the opera-

tion of pericardiolysis and also after excision of a portion of the sternum for removal of tumors of that bone. It has been observed in such cases that the tissues assume enough rigidity of their own so that the plaster plaque can be abandoned after seven to ten days. In these two children the use of this

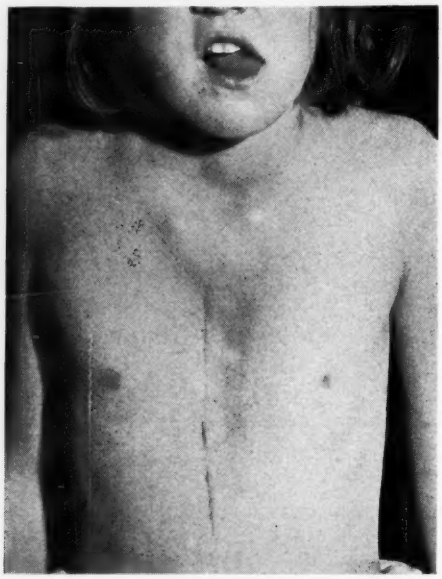

FIG. 14.—Case 2: View of chest three months after operation showing correction of deformity.

support was beneficial and appeared to eliminate the necessity for temporary external traction.

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BRACHIAL PLEXUS BLOCK ANESTHESIA: AN IMPROVED TECHNIC *

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THE INJECTION of local anesthetic agents into the brachial plexus for the production of regional anesthesia of the upper extremity is not new. Numerous descriptions,[1–20] have appeared in both the foreign and American literature since the original description by Crile,[1] in 1897, of a painless amputation of the upper extremity using this type of anesthesia. Nevertheless, this procedure has not gained widespread use especially in this country as evidenced by the failure of the cumulative index to record an American article on this subject prior to 1927.[2] Furthermore, it was employed in only 25 instances at the Mayo Clinic in 1940.[3] This lack of popularity is due to the frequent failure to obtain adequate anesthesia when the usual guide to the brachial plexus is used.

The landmark usually employed in reaching the brachial plexus, the midpoint of the clavicle, is not sufficiently accurate to insure contact with the plexus. Cases requiring anesthesia for a lesion of the upper extremity in which there also exists a contraindication to a general anesthetic are frequently encountered. This is especially true in injuries occurring in the Armed Forces. The purpose of this paper is to present a more accurate guide to the brachial plexus.

ANATOMY OF THE BRACHIAL PLEXUS

A study of the anatomy of the brachial plexus has been made in a series of neck dissections in postmortem specimens. These dissections showed a constant relationship between the anterior scalene muscle and the brachial plexus. Since this muscle is easily palpable in the neck, it should serve as an accurate guide to these nerves. Clinical application using this muscle as a guide has confirmed this impression. A total of 45 brachial plexus blocks has been carried out by five operators, with only three failures. This high incidence of successful anesthesia, 93 per cent, has been obtained by medical officers previously unfamiliar with this type of anesthesia. These results, we believe, are due to the relative ease with which the needle can be placed in contact with the brachial plexus when the anterior scalene muscle is used as a landmark.

The brachial plexus is formed by the lower four cervical nerves and a majority of the first thoracic nerve (Fig. 1). The primary anterior divisions

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of these spinal nerves unite to form three trunks which emerge into the posterior triangle of the neck between the anterior and middle scalene muscles three or four centimeters above the clavicle. These muscles arise from the transverse processes of the cervical vertebrae, the anterior scalene from the third, fourth, fifth and sixth, and the middle scalene from the transverse processes of the lower six cervical vertebrae. Each of these

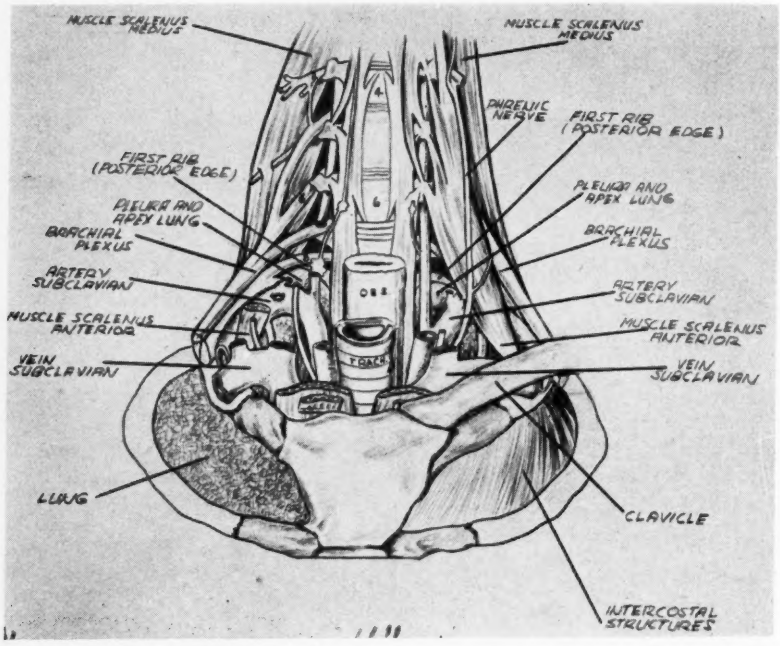

FIG. 1.—Anatomic sketch of an anteroposterior view of the neck illustrating the regional anatomy of the brachial plexus (Modified from Bailey, Surgery of Modern Warfare).

muscles is inserted into the first rib. The trunks of the plexus, namely the upper, middle, and lower, cross the middle third of the first rib and form an angle of approximately 23° with the lateral edge of the anterior scalene muscle. Thus, as these trunks pass through the posterior cervical triangle they remain relatively close to the lateral edge of this muscle. During their passage through the posterior triangle of the neck each trunk divides into two divisions preliminary to the formation of three cords. These cords are designated, lateral, posterior, and medial, according to their relationship to the subclavian artery. This artery also emerges between the anterior and middle scalene muscles just above their insertion into the last rib. The subclavian vein, however, lies anterior to the anterior scalene muscle; thus, the anterior scalene muscle separates the subclavian artery and vein (Fig. 2). The cords of the brachial plexus accompany the subclavian artery beneath the clavicle into the axilla to the lower border of the pectoralis minor muscle where they divide into their terminal branches.

The anterior scalene muscle can be located in the posterior triangle of the neck just above the clavicle by palpation. If the patient's head is turned toward the opposite side, flexed toward the shoulder (Fig. 3) and the fingers of the examiner's hand are drawn medially from the edge of the trapezius muscle just above the clavicle, a muscle mass will be felt just lateral to the clavicular head of the sternocleidomastoid muscle. The lateral edge of the most superficial muscle of this group, the anterior scalene, is the guide to the brachial plexus. The external jugular vein in most individuals runs from the

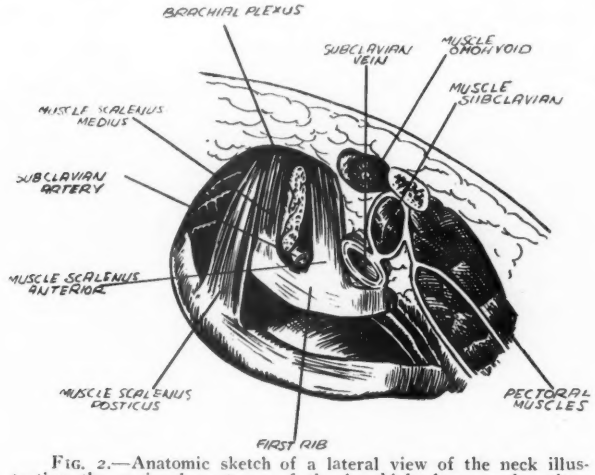

FIG. 2.—Anatomic sketch of a lateral view of the neck illustrating the regional anatomy of the brachial plexus and scalene muscles (Redrawn from Callander, Surgical Anatomy).

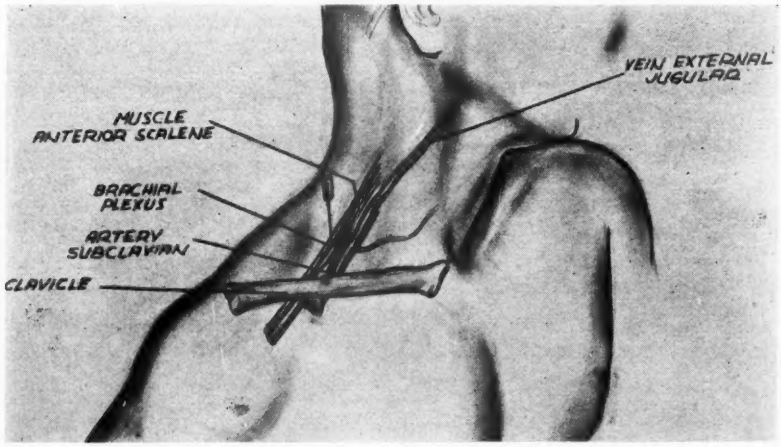

FIG. 3.—Sketch illustrating the relationships of the needle when properly inserted for injection of the brachial plexus. The position of the head is also demonstrated.

angle of the mandible to the midpoint of the clavicle and usually lies over the anterior scalene muscle in the region of the clavicle. This serves as an additional aid in locating the anterior scalene muscle. In thin individuals the plexus itself can occasionally be palpated as it traverses the posterior triangle.

TECHNIC OF PROCEDURE

After surgical preparation of the skin, with the patient's head in the position noted above, the lateral edge of the anterior scalene muscle is identified by palpation. Approximately 2 cm. above the clavicle, immediately over the lateral edge of this muscle, a small wheal is made in the skin with novocaine. An ordinary fine-caliber intravenous needle is inserted through the wheal and directed caudad, parallel to the midline, making an angle of from 30–45° with the skin of the neck (Fig. 3). Contact with the plexus is manifested by paresthesia in the arm or hand. When the needle contacts the nerves of the brachial plexus muscular twitchings of the forearm and hand occur. In unconscious patients this twitching can be used to ascertain the proper location of the needle prior to the injection of the novocaine. As soon as the needle is in the proper position 15–30 cc. of 2 per cent novocaine, containing 6 Mns. of adrenalin to the ounce, are injected. Care must be taken that the needle does not become misplaced during the injection. We have found it unnecessary to attempt to inject the individual trunks, cords, or nerves to obtain adequate anesthesia. It is recognized that the nerve supply of the skin of the proximal portion of the upper arm is not derived from the brachial plexus but from the intercostal nerves. If anesthesia of this area is necessary, one must encircle the upper arm with a subcutaneous injection of novocaine in addition to blocking the brachial plexus. Adequate anesthesia has resulted in 93.4 per cent of the cases in from 10–20 minutes. If the first rib is encountered without the production of paresthesia, the needle should be withdrawn and reinserted at a slightly different angle. Anesthesia is practically assured if definite contact with the plexus is made. The presence of the needle in the fascia surrounding the nerves is also evidenced by an increased resistance of the tissue to the needle. This resistance is easily recognized after a little experience. There is frequently, in addition to the above, a definite resistance to the injection of the solution. Occasionally when this resistance is marked, the patient will experience paresthesia during the injection.

We have found brachial plexus block well suited to a variety of surgical diseases of the upper extremity (Table I). It has been well suited to the surgical treatment of deep infections of the hand, in that it permits the use of a tourniquet and adequate exploration of the fascial spaces is possible. Its value in the treatment of fractures of the forearm and hand has been previously noted.[4, 5] It is particularly indicated in these injuries when an experienced anesthetist is not available or when the reduction is to be aided by the use of the fluoroscope. In the latter instance the hazards of an unconscious patient in the darkened fluoroscopic room are avoided. In addition, this type of anesthetic is particularly well suited to the repair of severed tendons. Following the injection of novocaine around the nerves of the plexus, pain is the first sensation to be abolished. This is subsequently followed by loss of the sense of touch. It is possible to have adequate anes-

TABLE I

Case No.	Diagnosis	Operative Procedure	Operative Time* (Minutes)	Anesthesia
1	Chronic tenosynovitis	Excision tendon sheath	40	Complete
2	Fracture, radius	Closed reduction	25	Complete
3	Ganglion, wrist	Excision of ganglion	75	Complete
4	Infected hand	Incision and drainage	30	Complete
5	Fracture, radial head	Manipulation and encasement	35	Complete
6	Chronic tenosynovitis	Excision tendon sheath	110	Complete
7	Onychitis, mycotic	Onychectomy	45	Complete
8	Giant cell tumor of the tendon sheath	Excision of tumor	25	Complete
9	Chronic olecranon bursitis	Excision of bursa	27	Complete
10	Compound fracture, finger	Débridement and reduction by skeletal traction	45	Complete
11	Severed tendon, flexor profundus, Fifth finger	Débridement and tenorrhaphy	80	Complete
12	Palmar abscess	Drainage of palmar abscess and exploration of thenar space	10	Complete
13	Burns, arm	Débridement and pressure dressing	72	Complete
14	Laceration, hand	Débridement	40	Complete
15	Giant cell tumor of the tendon sheath	Excision of tumor	30	Complete
16	Severed tendons	Tenorrhaphy	45	Complete
17	Severed tendons	Tenorrhaphy	105	Complete
18	Old severed tendons, with scar fixation	Tenoplasty	175	Complete None
19	Multiple verrucae, hands	Fulguration		Paresthesia not produced. Unsuccessful
20	Chronic bursitis, olecranon	Excision of bursa	28	Complete
21	Chronic bursitis, olecranon	Excision of bursa	114	Required local infiltration of skin for closure
22	Dupuytren's contracture	Excision of palmar fascia, partial	93	Complete
23	Severed tendons	Tenorrhaphy	55	Complete
24	Fracture, ulna & radius	Closed reduction	35	Complete
25	Fracture, ulna & radius	Insertion Haynes' pins	45	Complete
26	Chronic bursitis, olecranon	Excision of bursa	63	Complete
27	Severed tendon	Tenorrhaphy	33	Complete
28	Traumatic amputation, third & fourth fingers	Débridement and closure	70	Complete
29	Fracture, humerus	Haynes' pin fixation	70	Complete
30	Gunshot wound, hand, compound metacarpal fracture	Débridement, reduction and encasement	65	Complete
31	Lumbrical abscess	Incision and drainage	15	Complete
32	Fixation scar of tendon	Tenoplasty	85	Complete
33	Scar fixation, tendons of wrist	Tenoplasty	105	Complete
34	Ganglion, wrist	Excision of ganglion	30	Complete
35	Crushed hand	Débridement and amputation, first, second and third fingers	120	Complete
36	Crushed hand, blast	Débridement	305	Complete
37	Abscess, hand	Incision and drainage	None	Paresthesia obtained. No anesthesia
38	Denuded wound, hand	Full-thickness skin graft	70	Complete
39	Infected hand, human bite	Débridement, incision and drainage	None	Paresthesia not obtained. No injection
40	Painful amputated stump, finger	Reamputation, finger	50	Complete
41	Burns	Débridement, pressure dressing	120	Complete
42	Burns	Débridement, pressure dressing	120	Complete
43	Infected hand	Incision and drainage	15	Complete
44	Laceration, hand	Débridement and repair	65	Complete
45	Ganglion, wrist	Excision of ganglion	75	Complete

* Total duration of anesthesia was not determined; this represents the time in minutes adequate surgical anesthesia was present while in the operating room.

thesia and the sense of touch persist. The complete loss of sensation, both pain and touch, precedes the loss of motor function. Partially retained motor power is a very valuable aid in matching severed ends of tendons prior to their suturing.

Aside from the humane point of view, the relief of pain is essential to the successful treatment of shock. Clinical evidence indicates that pain is a stimulus to both the development and depth of shock. The relief of pain is, therefore, a valuable therapeutic measure. Pain arising in the upper extremity can be completely and quickly relieved by a brachial plexus block. This relief is more prolonged and complete than that afforded by opiates, without the associated anoxia resulting from respiratory depression. The cleansing and débridement of burns of the upper extremity can be painless and more quickly carried out with anesthesia. This type of anesthesia has worked well in these cases. Likewise, brachial plexus block is indicated in extremely painful lesions of the arm while preparations are being made for definitive treatment. This is illustrated by Case 36, Table I. This patient suffered a badly mangled hand following an explosion, and, on admission, was in extreme pain and shock. In spite of active shock therapy his general condition did not improve until the pain had been completely relieved by a brachial plexus block. This individual had previously received a total of one grain of morphine without relief. Immediately following relief of the pain by the block he responded to shock therapy, and it was possible to débride and close the wound. No supplementary anesthesia was necessary although a total of 305 minutes elapsed between the initial injection of novocaine and the completion of the operative procedure. The excellent result obtained in this case suggests the value of this procedure in the combat zone. Soldiers suffering from painful injuries of the upper extremities can be completely relieved by brachial plexus block prior to their transfer from forward stations. The relief thus obtained should be more lasting than that produced by large doses of morphine. A small dose of opiate can then be given for its euphoric action without depressing the respiration.

In this series of 45 cases anesthesia was not obtained three times (6.6 per cent). Failure to obtain anesthesia is usually due to one of the following:

1. Inactive novocaine solution.

2. Failure to use adrenalin in the solution, so that the novocaine is absorbed from the field before its fixation in the large nerve trunks. Braun[6] states that prior to the use of adrenalin it was impossible to produce this type of anesthesia for this reason. In this series we have made no effort to confirm or disprove this statement.

3. Failure to inject the novocaine in contact with the nerves.

In one of our unsuccessful cases contact with the plexus was not made, as evidenced by a failure to produce paresthesia. Novocaine was injected in the region of the first rib, as advocated by some operators[3, 7, 8] but anesthesia did not occur. In another of our three failures paresthesia did not occur

and no attempt was made to obtain anesthesia by blind injection around the first rib in this case. The other failure occurred after definite, unmistakable contact with the brachial plexus had been made. The cause for this failure was not apparent.

With all anesthetics there are certain dangers and secondary effects that must be constantly borne in mind if they are to be employed with a maximum of safety. Hartel and Keppler[9] found phrenic nerve paralysis was a regular accompaniment of brachial plexus block. The phrenic nerve passes through the neck on the ventral surface of the anterior scalene muscle (Fig. 1). Thus, it is relatively close to the field of injection and it is easy for the solution to spread to it. In this series, fluoroscopic examination performed after the operative procedure had been completed showed paralysis of the diaphragm in 20 per cent of the cases examined. In all instances the paralysis was temporary. In one instance, at the time of the fluoroscopic examination, there was a weakness of the diaphragmatic contractions, without a complete paralysis. Repeated fluoroscopic examinations on this patient revealed a complete recovery of the diaphragmatic movements before sensation returned in the arm. It is probable that paralysis of the diaphragm would have been found more frequently in this series of cases had the examination been made immediately after the injection rather than after the operative procedure was completed. It is certain that the paralysis is only transitory and is not as prolonged as the anesthesia. Hartel and Keppler, because of their findings relative to paralysis of the diaphragm, advised against a bilateral brachial plexus block. Strode[4] performed a bilateral upper extremity amputation with this type of anesthesia and noted no ill effects. In this series an officer, suffering from burns of both upper extremities, was débrided and a Koch's pressure dressing applied, without evidence of respiratory embarrassment under bilateral brachial plexus block.

In the above group of cases there have been no complications and no side-effects noted other than the phrenic paralysis as mentioned. In a review of the literature, however, the following additional complications have been observed:

1. Temporary paralysis of the cervical sympathetic chain with the development of a typical Horner's syndrome.[10]

2. Puncture of the dome of the pleura. It must be remembered that the pleura extends well above the first rib anteriorly (Figs. 1 and 2). Puncture is manifested by pain and dyspnea if sufficient air is allowed to enter the pleural cavity through the open needle. In one reported case[11] death was attributed to this accident. The entry of air into the pleura can be prevented, if the needle is inadvertently thrust into it, by keeping a syringe attached to the needle during its insertion.

3. Novocaine reaction, though rare, must always be borne in mind when utilizing this drug. The preoperative preparation of the patient with barbiturates makes this infrequent complication even more unlikely. There

is more danger of the development of a novocaine reaction if the tip of the needle is in the pleural cavity at the time of injection due to the rapid rate of absorption of novocaine from the pleura.

4. Anesthesia and paralysis persisted for three months in one reported case.[12] Whether this was due to trauma to the plexus by the needle or to an increased sensitivity to the drug with severe nerve damage is not known.

5. The accidental insertion of a needle into one of the great vessels has frequently occurred. This complication was dreaded by physicians early in the use of local anesthetics. It is now common knowledge that entry into a large vessel by a fine-caliber needle is a relatively innocuous procedure. It should be pointed out that care must be taken to determine that the needle is not in a major vessel prior to the injection of the solution.

SUMMARY

1. A new technic for injecting the brachial plexus to produce regional anesthesia of the upper extremity has been described.

2. A table showing the nature of the lesions treated, the types and duration of the operative procedures and the adequacy of the anesthesia have been included.

3. The complications noted in this series of cases and those reported in the literature are discussed.

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ANNALS OF SURGERY
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BASAL CELL LESIONS OF THE NOSE, CHEEK AND LIPS

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BASAL CELL LESIONS are most frequent about the nose, cheek and lip areas. Their study is not monotonous, however, because their etiology is variegated and the response of individual lesions to the different forms of therapy is far from uniform. Early lesions show hyperkeratoses of varying extent and flattened irregular nodular masses. If untreated they are apt later to become the so-called rodent ulcers. Most pathologists regard these tumors as growth derived from the lowermost or basal layers of the epidermis, for which reason they seldom show any tendency to keratinization or to pearl formation. Sections through such tumors show a complexity of downward-growing strands, all reaching to about the same level, sharply outlined against the stroma, and having very little inclination to strew cells into the irregular crevices of that tissue. This morphologic character is doubtless an expression of their relatively benign type of growth, and the rarity of any tendency to metastasize. Later on, however, necrosis and ulceration are common and the tumors often present themselves as slowly advancing ragged shallow ulcers with only a very thin wall of tumor tissue.

Etiologically, basal cell epitheliomata may start in some chronic growth or skin change; after an acute injury; after much exposure to strong light or to harsh winds and weather, as in the many cases occurring in farmers and sailors; after repeated roentgen ray treatments, such as for acne; or sometimes apparently spontaneously as a superficial red or pearly spot. Chronicity is usually an outstanding characteristic, but umbilication or ulceration may occur either early or late. In the occasional case *apparently* showing metastases to regional lymphodes or to some distant part of the body, a careful study will show that a squamous cell carcinoma has developed at the margin of a basal cell involvement and that the metastatic lesion is of squamous rather than of basal cell origin.

In early cases and in recurring ones in which the involvement and destruction have not been too extensive to make complete excision feasible, we prefer definite excision with the cold knife and such plastic repair as is adaptable to the situation. The recurrences are few and the cosmetic results are usually satisfactory.

It is true that many incipient and early basal cell lesions can be destroyed by caustics, cauterization, fulguration, desiccation, radium or roentgen ray.

* Read before the Annual Conjoint Meeting of the New York Surgical Society and the Philadelphia Academy of Surgery, Philadelphia, February 9, 1944.

To be safe by any method the destruction of the lesion must be complete. It is probable that both radium and roentgen ray are more efficient than caustics. The resulting defects from the use of some of the above-named methods are apt to leave more scarring than does a clean excision.

In basal cell lesions the fate of the patient rests largely on the judgment

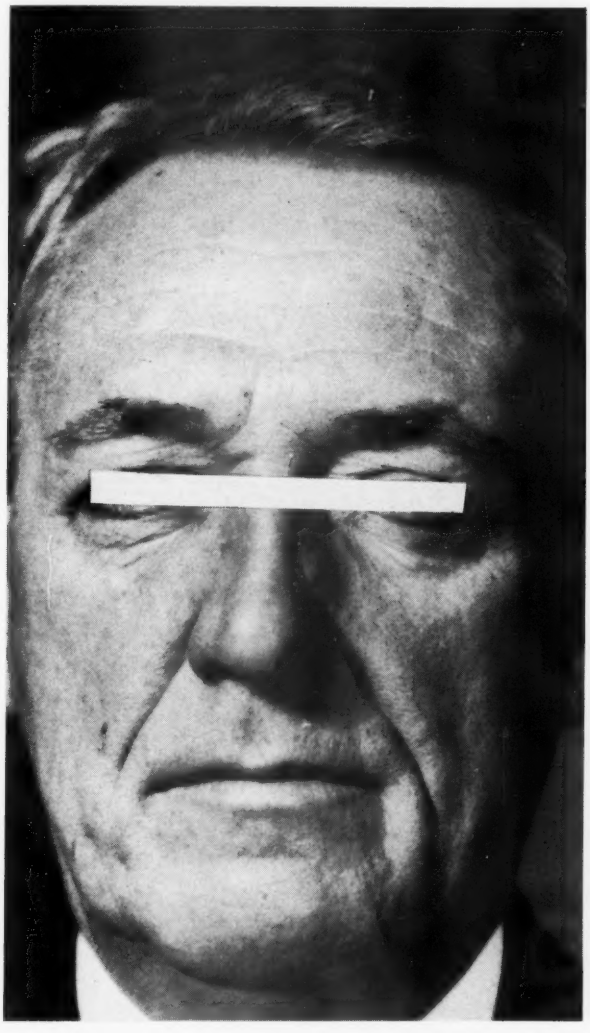

FIG. 1.—H. R., age 57: Showing appearance of nose four years after excision of basal cell lesion with beginning ulceration (1.5 × 1.3 cm.) from midportion of left nasal ala. Surrounding tissues were freely undermined and immediately approximated. The lesion had been demonstrable for five years before operation.

of the physician in charge during the early stages of the growth and his mastery of the method of treatment he first elects to employ. Some of the recurrences occur in cases which have been classed in the "cured" group for more than five years.

I have no statistics on the percentage of recurring basal cell lesions which have been treated by the various methods, but my personal impression is that the vast majority of them have at some time received roentgen ray treatments. Those referred to us for plastic repair have usually had one or more recurrences, with repeated treatments. Often there has been considerable destruction of tissue and much fibrosis surrounding the area. The fibrosis is

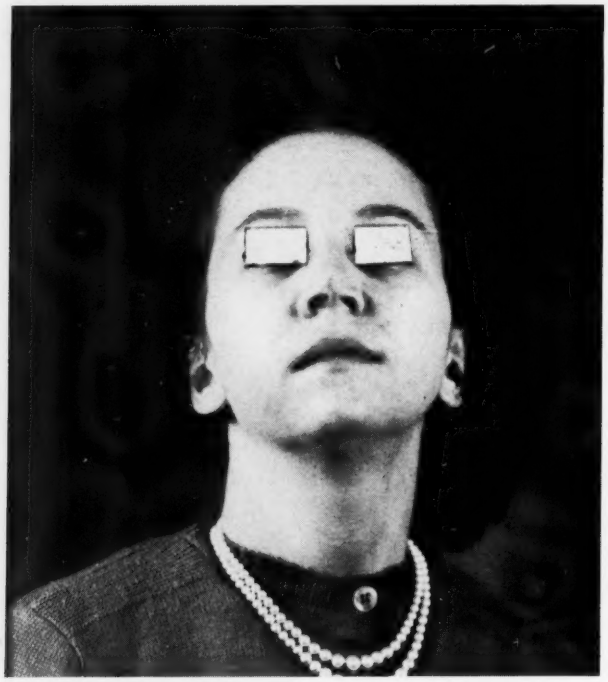

FIG. 2.—D. S., age 32: Showing appearance of tip of nose two years after excision of basal cell ulcer (1 × 1.25 cm.) from tip of nose. Full-thickness skin graft from postauricular region was immediately applied. (The lesion resulted from repeated roentgen-ray treatments for acne).

a definite handicap in plastic repair because of the decreased blood supply. While the eradication of the basal cell area is, of course, the primary consideration, the ultimate cosmetic appearance deserves careful consideration because of the psychologic and economic results. Thus, when it is found that the cells are not responding to radiation therapy as satisfactorily as expected, would it not be wiser, when the location of the lesion is favorable, to utilize surgical excision and plastic repair while the surrounding tissues are not too fibrosed and still have an adequate blood supply?

In advanced cases with wide and deep ulcerations, which tend to recur soon after what is regarded as adequate radiation therapy, plastic reconstruction is usually not feasible. In such cases the use of suitable prostheses minimize the patient's mental depression and permit social contacts for varying periods of time.

FIG. 3.—F. H.—4683, age 54: A and B. Appearance of left infra-orbital area one year after excision of basal cell ulceration (1.5 × 2 cm.) and advancement of large triangular flap from the lateral nasolabial fold.

Lantern slides from gloss-finished unretouched photographs show the results obtained by the following procedures:

1. Excision followed by undermining surrounding skin and approximation of the margins. (Fig. 1).

2. Excision and immediate full-thickness free skin graft (Fig. 2).

3. Excision and use of single pedicled flap from lateral nasolabial fold (Fig. 3).

4 A

4 B

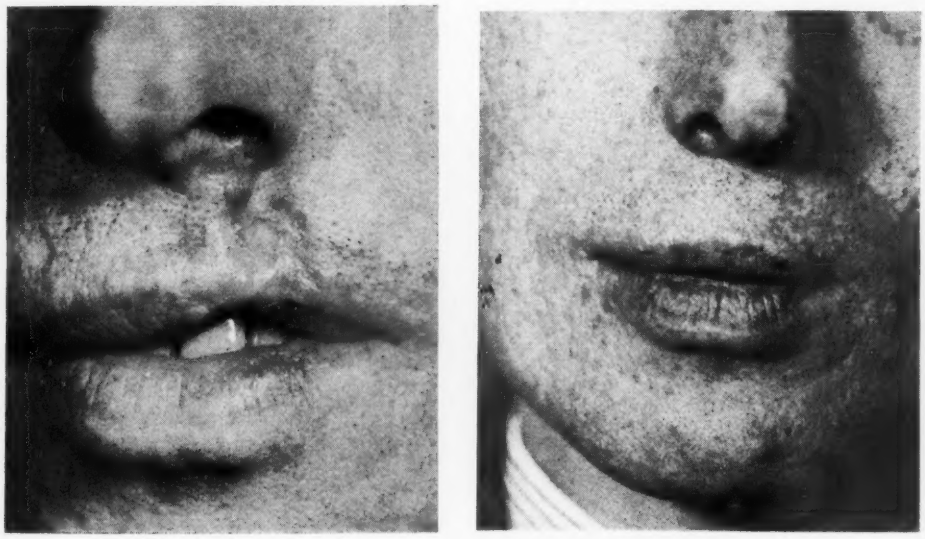

FIG. 4.—E. H.—6711, age 35

A. Basal cell lesion of lip. Result of roentgenray treatments for acne over a period of four years.
B. Appearance of lip two years after excision of over one-third of lip and advancement of flaps.

4. Excision and advancement of flap from lip and cheek (Fig. 4).

5. Excision and use of delayed frontal pedicled flap, double epithelized (Fig. 5).

5 A 5 B

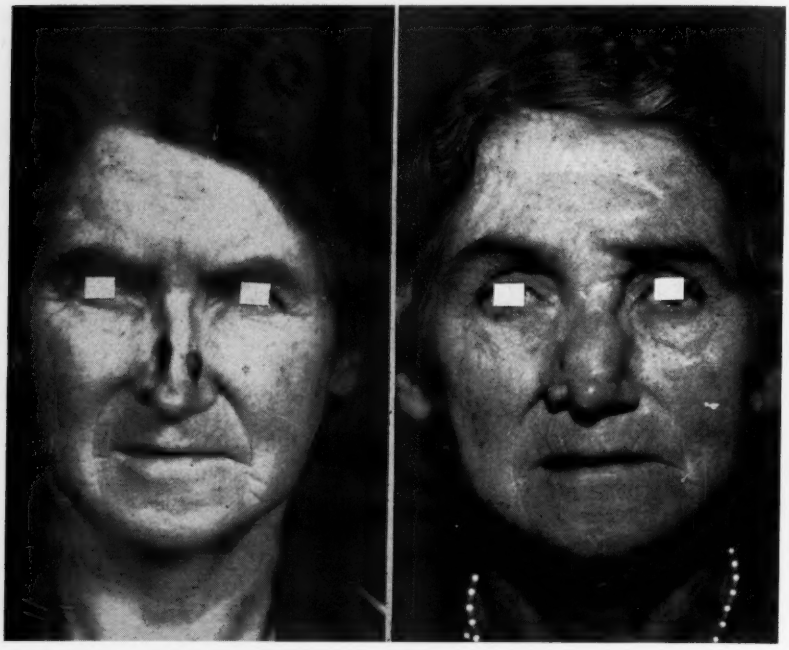

FIG. 5.—F. H.—6331, age 60

A. Basal cell ulcerations of dorsum of nose of 28 years duration.

B. Appearance of nose two years after excision of involved portion and reconstruction by use of double epithelized frontal flap.

CONCLUSIONS

1. Basal cell lesions are characterized by their chronicity, slow local progress, absence of metastases to local or distant areas.

2. The most important point in treatment is completeness of removal in the primary attempt—whatever method is employed.

3. In early and moderately advanced lesions, excision and plastic repair offer good chances for cure with minimum disfigurement.

4. In late repeated recurrences with marked destruction of tissue, a prosthesis may be preferred to plastic procedures.

EFFECT OF LOCALLY IMPLANTED SULFONAMIDES ON WOUND HEALING

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DURING THE PAST FEW YEARS there has been an increasing enthusiasm for the implantation of sulfonamides locally in wounds. The local use of sulfonamides has become so popular that many surgeons not only use it in cases that are likely to become infected, but they use it routinely in all of their operative wounds.[1-4] When an agent is used routinely in all operative procedures, it is the surgeon's duty to be absolutely certain that the agent employed does not do more harm than good. One way in which local sulfonamides might do harm is by interfering with wound healing. It has long been recognized that foreign bodies delay the healing of wounds. Although sulfonamide crystals apparently excite no specific type of cellular reactions in wounds, they must be regarded as foreign bodies and they do cause a foreign body reaction as long as they remain in the crystalline or powder form. Certain sulfonamides in high concentrations are known to be toxic to human cells. Jacoby, Medawar and Willmer[5] have demonstrated the toxicity of sulfanilamide and sulfathiazole to human cells in tissue cultures. Reed, Orr and Anderson[6] have shown that sulfathiazole in high concentration inhibits the growth of fibroblasts, This toxicity is recognized by a suppression of growth and lack of multiplication of fibroblasts, macrophages, and epithelial cells.

Opinions differ as to the actual effect of sulfanilamide and sulfathiazole on wound healing. Bricker and Graham[7] reported that systematically administered sulfanilamide interferes with wound healing. This was contrary to the findings of Zintel, *et al.*,[8] who found that systemic sulfanilamide and sulfadiazine did not interfere with wound healing. Taylor[9] feels that the use of all sulfonamides when implanted locally in wounds produces such profound inflammatory reactions that their employment is not justified. Bick[10] reported that, in his experience, the use of sulfonamides locally in primary sutured wounds of the soft parts retarded wound healing by at least 50 per cent of the time factor, and that they caused extensive cutaneous scarring. On the other hand, Glynn[11] reported that sulfathiazole and sulfapyridine inhibit fibroblastic proliferation, and that sulfanilamide and sulfapyridine have a definite toxic action on striped muscle, but that these effects are not sufficient to contraindicate the use of these drugs. Harbison and Key,[12] and Key[4] have reported that the local implantation of sulfanilamide and sulfathiazole in moderate amounts does not interfere with wound healing. Taffel and Harvey[13] have reported that systemically administered sulfanilamide did not retard the healing of stomach wounds in rats. Considering

the apparently conflicting reports, it seemed appropriate to repeat the experiments using sulfanilamide and sulfathiazole locally in uninfected wounds. In the experiments mentioned, no attempt was made accurately to control the amount of sulfonamide placed in the experimental wounds. In this experiment the amount of sulfonamide deposited in the wound was carefully controlled. The amount used was equivalent to one gram for each ten square inches of wound surface.

Measurement of the degree of wound healing resolves itself into three main phases, namely: Clinical course, including the resultant cosmetic effect of the degree of scarring; tensile strength; and histologic structure of wounds during the course of healing. The reported clinical observations have not been generally satisfactory because of the lack of an adequate number of control cases. Few surgeons have been willing to use alternate cases as controls. The data published here are from experimental wounds in animals. In such wounds not only the clinical course, but also the tensile strength, and histologic structure can be studied through the entire period of wound healing. Measurement of the tensile strength and microscopic studies during the period of wound healing, offer a more direct method of evaluating the degree of wound healing.

The purpose of this experiment was to test the effect of locally implanted sulfanilamide and sulfathiazole on wound healing. Both the microcrystalline* and the macrocrystalline forms of sulfathiazole were used. Uniform amounts of these agents were used. It is well known that large amounts of sulfonamides in wounds not only cause caking of the sulfonamides, but also cause serum collections which interfere with wound healing.

Four groups of 12 rats each were used. The first group was the control group. The second, third and fourth groups had implanted in their wounds, sulfanilamide, microcrystalline sulfathiazole and macrocrystalline sulfathiazole, respectively. Incisions exactly four centimeters long were made through the entire thickness of the abdominal wall, four millimeters lateral to, and parallel to, the linea alba. After closing the peritoneum and transversalis muscle with a continuous suture of plain No. 00000 catgut to amount of sulfonamide equivalent to one gram per ten square inches of wound surface was placed in the wound. Thus, the amount deposited in a wound four centimeters long in an abdominal wall three millimeters thick, was 37 milligrams. The crystals were spread as evenly as possible over the wound surface. The remaining muscular and fascial layers of the abdominal wall were closed with a continuous plain No. 000 catgut suture. Approximation of the skin was by means of interrupted silk sutures. Treatment of the control animals was exactly the same except that no sulfonamide was introduced into the wounds.

* Provided by Smith, Kline, and French, Inc. The so-called microcrystalline sulfathiazole has a particle size of five to six microns as compared with a particle size of 30 microns for the ordinary sulfathiazole preparations, here called macrocrystalline sulfathiazole.

Three animals of each of the four groups were sacrificed on the 4th, 8th and 12th postoperative days. After the removal of the silk sutures the tensile strength of the entire thickness of the abdominal wall was determined by means of the tensiometer, as described in previous publications by Meade[14] and Zintel.[8] Blocks of tissue were prepared for microscopic study of all the wounds.

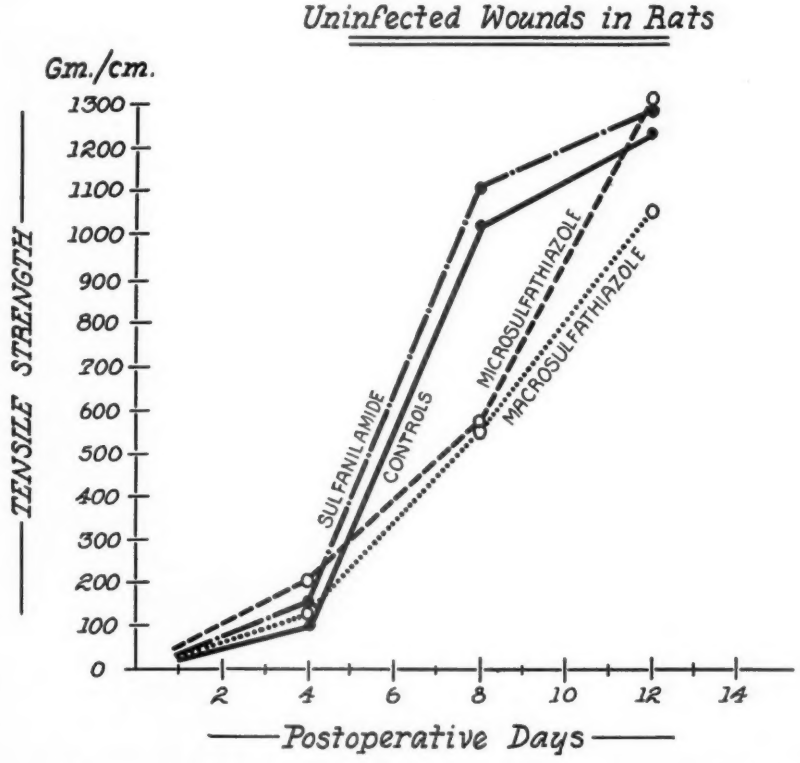

CHART 1.—Graphic demonstration of the tensile strengths of the various groups.

RESULTS.—No significant difference was noted histologically between the sulfonamide treated wounds and the control wounds. Evidences of slight infections occurred with equal frequency in both the experimental and the control animals. The reaction around the remaining fragments of catgut did not vary from one group to the other. Microscopically, no significant difference was noted in the incidence or degree of infection; in the reaction to catgut; in the extent of fibroplasia; or in the degree of epithelization.

The tensile strengths of the various groups are shown graphically in Chart 1. Four days after operation there was no difference in the tensile strengths of the control and sulfonamide-impregnated wounds. On the eighth postoperative day the tensile strengths of the wounds that were treated with sulfathiazole (both the macrocrystalline and the microcrystalline forms) were definitely less than the tensile strengths of the control and sulfan-

ilamide-treated wounds. At the end of 12 days the tensile strengths of the wounds in all groups were normal except the group which was impregnated with macrocrystalline sulfathiazole. The macrocrystalline sulfathiazole-impregnated wounds were not so strong as the wounds of the control animals on the 12th postoperative day.

Sulfanilamide, therefore, when implanted in wounds in amounts equivalent to one gram per ten square inches of wound surface, did not retard wound healing. Wounds impregnated with an equivalent amount of the ordinary form of sulfathiazole were definitely weaker than the wounds of the control and sulfanilamide-impregnated wounds. Wounds impregnated with microcrystalline sulfathiazole were not so strong as the control animals on the eighth day, but these wounds attained normal strength on the 12th postoperative day.

A possible explanation of the fact that sulfathiazole inhibits wound healing when applied locally, and that sulfanilamide does not significantly inhibit wound healing, lies in their difference of solubility. Both substances have been shown to be toxic to human cells in tissue cultures. Sulfanilamide being the more soluble of the sulfonamides tested, disappears from wounds quite rapidly. Sulfathiazole being less soluble, remains in wounds longer, and, therefore, exerts its toxic action and causes a foreign body reaction for a longer period of time. This period is apparently prolonged enough to delay healing of the normal wound. The microcrystalline form of sulfathiazole is more readily soluble than the ordinary macrocrystalline sulfathiazole by reason of its greater surface area. Apparently the "toxic" action following the implantation of microcrystalline sulfathiazole is sufficiently prolonged to interfere with the tensile strength of healing wounds on the eighth postoperative day, but it is not sufficiently prolonged to interfere with wound healing at the end of 12 days. The detrimental effect of macrocrystalline sulfathiazole is still apparent at the end of 12 days, suggesting that the microcrystalline form is better tolerated than the macrocrystalline form of sulfathiazole. The results here reported would indicate that sulfathiazole should not be implanted into operative wounds if maximal wound healing is desired. Sulfanilamide crystals do not interfere with wound healing when evenly applied to wounds in amounts equivalent to one gram per ten square inches of wound surface.

CONCLUSIONS

1. It has previously been demonstrated that sulfonamides are toxic to some human tissue cells.

2. Our previous experiments indicate that therapeutic concentrations of systemically administered sulfanilamide and sulfadiazine do not interfere with the healing of the uninfected wound.

3. Sulfanilamide in amounts equivalent to one gram per ten square inches of wound surface does not interfere with normal wound healing.

4. Microcrystalline sulfathiazole (particle size five to six microns)

implanted locally in wounds, produces wounds with a decreased tensile strength at eight days, but the tensile strength of these wounds is normal at the end of 12 days.

5. Macrocrystalline sulfathiazole, the commonly used form of sulfathiazole, causes a delay in wound healing which is apparent even at the end of 12 days.

The author wishes to acknowledge assistance from Dr. Souther Tompkins during a portion of this study.

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ANESTHETIC DEATHS IN 54,128 CONSECUTIVE CASES

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DURHAM, N. C.

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IN AN ENDEAVOR to evaluate the safety of the various anesthetics in our hands we have analyzed all cases of sudden death occurring on the operating table at Duke Hospital during a 12.5-year period. The difficulty in assessing the part played by the anesthetic in the death of a patient during or following operation is well known and the difficulty increases in proportion to the time elapsing between the operation and the patient's demise. We have limited our study, therefore, to those cases in which death occurred during or shortly after operation.

From July 1, 1930, to January 1, 1943, a total of 54,128 anesthesias were administered for all types of operative procedures. During this period 38 patients died during operation or a few minutes thereafter (Table I). Twenty-seven deaths which are ascribed to the anesthesia (Table II) occurred during general or spinal anesthesia. Some of the patients undoubtedly would have succumbed sooner or later to the existing disease but the anesthesia could not be completely exonerated as the immediate cause of death.

TABLE I

Anesthetic	Total No. of Anesthesias	Total No. of Sudden Deaths	No. Per 1000 Anesthesias	Anesthetic Deaths	No. Per 1000 Anesthesias
Ether	14,724	6	.407	6	.407
Cyclopropane	5,744	7	1.21	4	.691
Cyclopropane with ether	393	0	0	0	0
Nitrous oxide	6,705	4	.590	2	.295
Nitrous oxide with ether	2,175	2	.919	2	.919
Ethylene	6	1		1	
Chloroform	9	0	0	0	0
Vinethene	266	0	0	0	0
Vinethene with ether	326	0	0	0	0
Avertin	261	1	3.83	1	3.83
Avertin with supplement	1,615	6	3.71	3	1.85
Sodium pentothal	1,006	1	.99	0	0
Sodium pentothal with nitrous oxide	226	0	0	0	0
Evipal	48	0	0	0	0
Spinal	5,436	6	1.10	6	1.10
Spinal with supplement	930	2	2.15	2	2.15
Caudal	1,106	0	0	0	0
Local	13,151	2	.150	0	0
Sodium amytal	4	0	0	0	0
Total	54,128	38	.702	27	.498

TABLE II

CAUSE OF DEATH IN 38 CASES OF SUDDEN DEATH ON THE OPERATING TABLE

Shock	2	
Hemorrhage	2	
Infection	5	
Medullary compression	2	
Asphyxia due to aspiration of vomitus	1	Anesthetic deaths
Unknown	26	Anesthetic deaths
Total	38	

TABLE III

ANALYSIS OF ANESTHETIC DEATHS IN 39,880 CASES OF GENERAL AND SPINAL ANESTHESIA

			Sex		Race		Operative Risk		
	Case	Age	Male	Female	White	Colored	Good	Poor	Autopsy
Ether	1	50		+	+		+		0
Ether	2	2	+		+		+		0
Ether	3	8	+		+		+		0
Ether	4	7 wks.		+		+	+		0
Ether	5	21	+			+	+		0
Ether	6	30	+			+	+		+
Cyclopropane	7	11		+		+	+		+
Cyclopropane	8	17	+			+	+		0
Cyclopropane	9	17	+			+	+		+
Cyclopropane	10	26	+		+			+	0
Nitrous oxide	11	49	+			+		+	+
Nitrous oxide	12	55	+			+		+	+
Nitrous oxide-ether	13	36		+		+		+	+
Nitrous oxide-ether	14	29		+		+		+	0
Ethylene	15	28		+		+		+	+
Avertin	16	25	+			+		+	+
Avertin-ether	17	20		+		+	+		0
Avertin-ether	18	33	+			+	+		+
Avertin-ether	19	16	+			+	+		0
Spinal	20	37	+		+			+	0
Spinal	21	50		+		+		+	0
Spinal	22	31	+			+		+	+
Spinal	23	62	+		+			+	+
Spinal	24	39	+			+		+	0
Spinal	25	53		+	+			+	0
Spinal with supp.	26	41		+	+			+	+
Spinal with supp.	27	63	+		+			+	0
Total	27		17	10	9	18	12	15	12

Eighteen of the 27 deaths, or 66 per cent, were in Negroes (Table III). This is significant in view of the fact that less than 15 per cent of the total number of patients undergoing operation annually at this hospital are Negroes. The explanation for this high mortality rate probably lies in the difficulty of judging the degree of cyanosis in colored individuals and in the poorer general condition of the average Negro as contrasted to the average white patient in the Duke Hospital.

It is interesting to note that of the six patients (Cases 1–6) who died during ether anesthesia (Table III) four were receiving *ether* through oral catheters and three of the latter were undergoing operations upon the eye. The combination of draping necessary for eye operations and the administration of ether vapor through a catheter makes it difficult for the anesthetist to judge the depth of anesthesia and the degree of cyanosis. The deaths,

except for one due to aspiration of vomitus, probably were due to overdosage. In 2,200 cases of general anesthesia, excluding cyclopropane, Schmidt and Waters[10] report two anesthetic deaths, one of which occurred during an eye operation in which the patient was receiving ether through an endotracheal catheter.

TABLE IV

COMPARATIVE STUDY OF ANESTHETIC DEATHS

*From the Literature**

Anesthesia		Total No. of Cases	Anesthetic Deaths	No. Per 1,000
General and spinal	Schmidt & Waters[10]	4,400	3	.681
	Dealy[4]	19,529	18	.921
	Duke Hospital	29,880	27	.677
Cyclopropane	Schmidt & Waters[10]	2,200	1	.454
	Sahler, *et al.*[9]	7,120	0	0
	Taylor[11]	39,284	10	.254
	Duke Hospital	5,744	4	.691
Avertin with supplement	Beecher[1]	3,934	7	1.78
	Mueller[8]	5,000	0	0
	Duke Hospital	1,615	3	1.85
Spinal	Dealy[4]	3,193	7	2.19
	Veal & Van Werden[13]	33,811	30	.887
	Duke Hospital	6,366	8	1.25

* No really accurate comparison of statistics is possible since there are such wide variations in nutritional states, conditions requiring operation, color (the "anesthetic" death rate is over ten times greater in the colored than in the white patients in the Duke Hospital), distances traveled, *etc.*

Autopsy performed upon the patient who died during herniorrhaphy (Case 6) revealed a partial occlusion of the right coronary artery by a sclerotic plaque. Follis[5] reports three consecutive cases of sudden death during nitrous oxide-oxygen-ether anesthesia in which a similar condition was found.

Two deaths in our *cyclopropane* series (Cases 7 and 9) appear to have been due to overdosage and in another (Case 8) overdosage could have been responsible for death. At autopsy, one patient (Case 7) was found to have a "granulomatous myocarditis," the significance of which is unknown. In retrospect, the choice of anesthesia for the patient with thyrotoxicosis (Case 10) was poor in view of the likelihood of the occurrence of ventricular fibrillation in this condition following the administration of cyclopropane.[2]

Both patients who died while receiving *nitrous oxide* were classified as poor operative risks. Perhaps an anesthetic permitting the use of a higher percentage of oxygen would have been a better choice for the individual with pulmonary tuberculosis (Case 11). There is still some disagreement over the choice of anesthesia in Ludwig's angina (Case 12). Trout[12] favors pentothal or ethylene, but adds that the surgeon should be ready to perform an emergency tracheotomy before the anesthesia is started and should stand by during the induction of the anesthesia. Bennett[3] recommends intratracheal intubation before operation. If this can be done any anesthetic agent is satisfactory.

The patients who expired while receiving a mixture of nitrous oxide-oxygen-ether (Cases 13 and 14) were poor operative risks, and it is difficult to say whether another type of anesthesia would have been a better choice.

Our experience with *ethylene* has been too limited to warrant comment. The one death (Case 15) is included in this study although shock appears to have been the more likely cause of death.

It is doubtful whether the patient who died under *avertin* anesthesia (Case 16) could have withstood the operation under any other type of anesthesia.

Avertin supplemented with ether has proved to be the most dangerous of all anesthesias in our hands. Three deaths have occurred in young adults considered good operative risks (Cases 17–19). The dangers of avertin used alone or as a basal anesthetic are generally recognized,[1] and in our experience its disadvantages appear to outweigh its advantages; its use, therefore, at the Duke Hospital has been discontinued except for an occasional case.

All deaths which occurred during spinal anesthesia at this hospital were in patients judged poor operative risks who were undergoing emergency abdominal operations (Cases 20–27). Perhaps the high mortality rate could be bettered by the judicious administration of fluids and careful continuous observation of blood pressure. At the present time special care is taken to insure constant blood pressure observation, and it is routine for intravenous fluids to be administered during all operative procedures of any length requiring a general or spinal anesthesia. Despite the high immediate mortality experienced when employing spinal anesthesia in emergency abdominal surgery, there are certain conditions which some feel demand this type of anesthesia. Graham and Brown[7] feel strongly that if adequate facilities are available spinal anesthesia should be used for all operations for acute intestinal obstruction. Foss and Bush[6] believe the risk of spinal anesthesia in cases where there is likelihood of extensive trauma to the viscera under general anesthesia is more than offset by the decreased risk resulting from the lessened visceral trauma made possible by the more complete relaxation. These views are opposed by Wangensteen,[14] however, who feels that in spite of certain advantages afforded by spinal anesthesia inhalation anesthesia offers the greatest safety to the patient suffering from intestinal obstruction.

SUMMARY

1. During 54,128 anesthesias of all types there have been 38 sudden deaths, or 0.702 per 1,000.

2. Twenty-seven so-called "anesthetic" deaths have occurred during 39,880 general and spinal anesthesias, or 0.677 per 1,000.

3. Two-thirds of the "anesthetic" deaths occurred in Negroes although

less than 15 per cent of the total number of patients undergoing operation annually at the Duke Hospital are Negroes.

4. If the ages and preoperative conditions of the patients who died are taken into consideration in evaluating the results, the most dangerous agents in our hands have been avertin-ether, with a death rate of 1.85 per 1,000, and cyclopropane, with a rate of 0.691 per 1,000.

5. The administration of ether through an oral or tracheal catheter to patients whose faces are obscured by heavy drapes is a dangerous practice.

6. Spinal anesthesia in debilitated, acutely ill patients with low blood pressure may hasten the end, but offers certain advantages not found in other types of anesthesia.

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BRIEF COMMUNICATIONS

TRAUMATIC RUPTURE OF THE GALLBLADDER

ROYAL F. SENGSTACKEN, M.D.

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TRAUMATIC RUPTURE of an apparently normal gallbladder is a very rare injury, but such a case was admitted to the Surgical Service, Good Samaritan Hospital, January 30, 1944. Frankly, it was not recognized as such until operation, 40 hours later. The outstanding difference between it and rupture of the other viscera we have seen, was the absence of any early signs of shock or of an acute surgical abdomen. In the past year we have been actively associated with cases of traumatic rupture of the spleen, kidney, liver, and small bowel (ileum), and in all these cases the onset of acute signs and symptoms was rapid.

Survey of the literature reveals less than 50 reported cases of traumatic rupture of the gallbladder from a blow on the abdominal wall. In fact, most of the earlier reported cases were never proved by operation or autopsy—simply diagnosed by aspirating quarts of bile, associated with peritonitis following abdominal injury. In these cases, also, the appearance of the acute surgical abdomen was slow, and the degree of shock varied according to the type and severity of the accident.

The case presented herewith is especially instructive as it was masked by intoxication. The patient being noisy and apparently not much hurt was almost not admitted to the hospital, as it was midnight and the admitting office did not wish to disturb the ward patients.

Case Report.—L. H., male, age 28, had been drinking rather heavily and ran his automobile into a tree. Presumably, he struck his upper abdomen against the steering wheel. He was brought from the scene of the accident to the hospital. The patient was noisy and non-cooperative, complained of no particular pain, and showed no signs of injury except a few scratches and slight contusions. Fortunately, the Resident ordered him put to bed, and he finally fell asleep after three hours, with the aid of sedatives.

He was still sound asleep the next morning, and as his T. P. R. were practically normal he was not disturbed. Later in the day his condition was reported as satisfactory, his only complaint being some abdominal soreness. The following morning, however, he was definitely sicker and his abdomen was becoming tender and somewhat rigid. The W. B. C. and polymorphonuclears were elevated. He had no nausea or vomiting and no blood in urine or stools. By afternoon his condition had become worse; Temperature 102.4° F., W. B. C. 25,000, polys 88 per cent. Lungs clear. Immediate operation was performed.

Operation.—Under spinal anesthesia, a right rectus incision was made part above and below the umbilicus. At once we remarked the yellow color of the peritoneum, and on incising it much free bile escaped. Careful exploration revealed no abnormalities until the finger entered what seemed to be the gallbladder. The incision was prolonged upward and the gallbladder exposed, revealing a rent 3 cm. long in the fundus on the side adjacent to the liver. The gallbladder appeared normal otherwise, and there were no signs of injury to the liver or bile ducts. The tear was sutured and sulfanilamide powder was sprinkled about it. One cigarette drain was placed in the abdomen in closing.

The patient had moderate distention and fever for 48 hours, and slight drainage of bile for 96 hours, but otherwise made a rapid, uneventful, and excellent recovery.

BOOK REVIEW

SURGICAL ERRORS AND SAFEGUARDS. By Max Thorek, M.D., LL.D., D.C.M., F.I.C.S.: With a foreword by Sir Hugh Devine, M.S., Hon. F.R.C.S. (Eng.), F.R.A.C.S., F.A.C.S. (Hon.), and a chapter on Legal Responsibility in Surgical Practice by Hubert Winston Smith, A.M., M.B.A., L.L.B., M.D., 4th ed. Philadelphia, Montreal, and London: J. B. Lippincott Co., 1943.

The new edition of Doctor Thorek's "Surgical Errors and Safeguards" has been entirely reset and considerably enlarged. The fact that it is issued as a fourth edition indicates that it has found a wide field of usefulness to the medical profession. It is particularly opportune that the fourth edition comes at this time. With the intern and resident system placed on a "9–9–9" basis there will be very little opportunity for the recent graduate to acquire a reasonably complete hospital training. There will be large gaps in the teaching program and very little time for a first class clinical experience. Therefore, a text-book that presents in an incisive fashion the possible errors and complications in diagnosis, preoperative, operative technic, and postoperative treatment, is more than welcome. The book itself is encyclopedic in scope, with many and extensive quotations from current surgical literature. A very complete and detailed index makes it possible for the student to have quick access to the particular problem that may be presented to him.

The text is presented in the form of innumerable paragraphs and does not lend itself for continuous reading. However, the intent of the author is not to write a discursive book on surgery but to indicate the high points of technical surgery, both from his own personal experience and that of others. At the end of each chapter is an extensive reference to the sources of the material. This feature should be of great value to the group of young men who will become the surgeons of the future. The selection and the quality of the material are on the whole excellent and the general tenor of the bibliography is to round out the high points of the preceding text.

The reviewer has very few criticisms. It would seem wise, however, for any future editions to submit the text and illustrations to a more critical selection. There are numerous illustrations that have no relationship to the text and aside from being reproductions of photographs have very little value. The inclusion of many of the statistical quotations is redundant and could well be omitted.

Section 19, "Legal Responsibility for Surgical Practice Based on Legal Doctrine in the United States and Great Britain," by Mr. Hubert Winston Smith of the Harvard Law School, is a valuable addition. The doctor in his professional capacity may commit one of several torts recognized by law and render himself liable to a civil action for damages. The contribution of Mr. Smith is presented briefly and with lucidity and projects the many intricacies of the law in relationship to the practicing surgeon.

It is a great pleasure to read the foreword by so eminent a surgeon as Dr. Hugh Devine of Melbourne, Australia, and the reviewer subscribes to this statement from the foreword: "This book is written with the intention to help, much as a surgeon father would wish to help a surgeon son, and as the guilds of the Middle Ages passed on their secrets from generation to generation."

The fourth edition of Doctor Thorek's "Surgical Errors and Safeguards" is an excellent book. It undoubtedly fulfills the purpose for which it is designed and is a credit both to the author and the publishers. The reviewer recommends it.

CHAS. GORDON HEYD, M.D.

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JUNE, 1944 Vol. 119, No. 6

ANNALS of SURGERY

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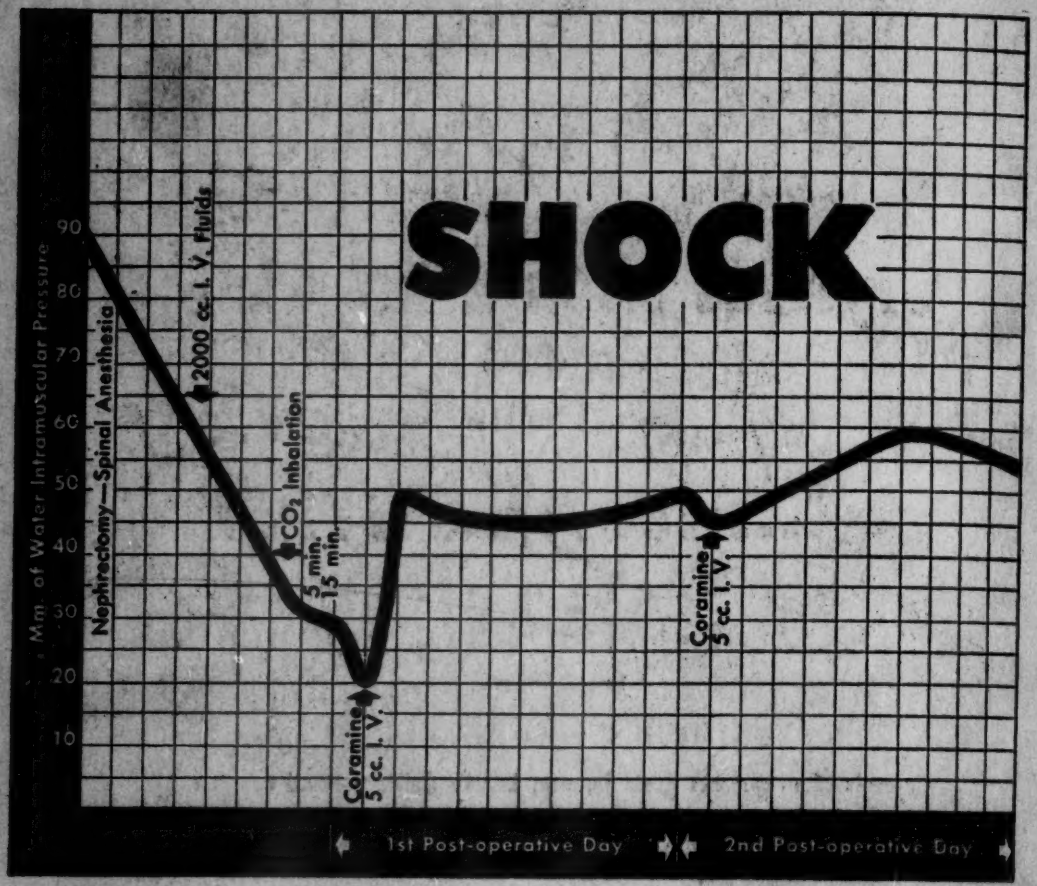

SHOCK is a complex syndrome having many causes and presenting many symptoms. Recent research[1] has demonstrated that in post-operative and post-anesthetic shock *intramuscular pressure drops before venous pressure fails.* This intramuscular pressure is of greatest importance in maintaining peripheral circulation and venous pressure is returned to normal by a restoration of intramuscular pressure.

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[1]Gunther, Lewis, Engelberg, Hyman and Strauss, Ludwig., INTRAMUSCULAR PRESSURE, Am. J. Med. Sci., 204, 266-283, Aug., 1942.

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